COMPARISON OF DEXMEDETOMIDINE AND LIDOCAINE IN PREVENTING COUGH DURING EMERGENCE FROM GENERAL ANAESTHESIA FOR THYROIDECTOMY – A RANDOMISED CONTROLLED TRIAL

Dissertation submitted in partial fulfillment of the requirement of the Tamil Nadu Dr. M.G.R. Medical University for M.D Branch X (Anaesthesiology) Examination to be held in May 2018.

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This is to certify that the dissertation entitled **"**Comparison of Dexmedetomidine and Lidocaine in Preventing Cough During Emergence from General Anaesthesia for Thyroidectomy – A Randomised Controlled Trial" is a bona fide original work of Dr. Charles J, towards the M.D. Branch X (Anaesthesiology) degree examination of the Tamil Nadu Dr. M.G.R. Medical University, Chennai, to be conducted in May 2018.

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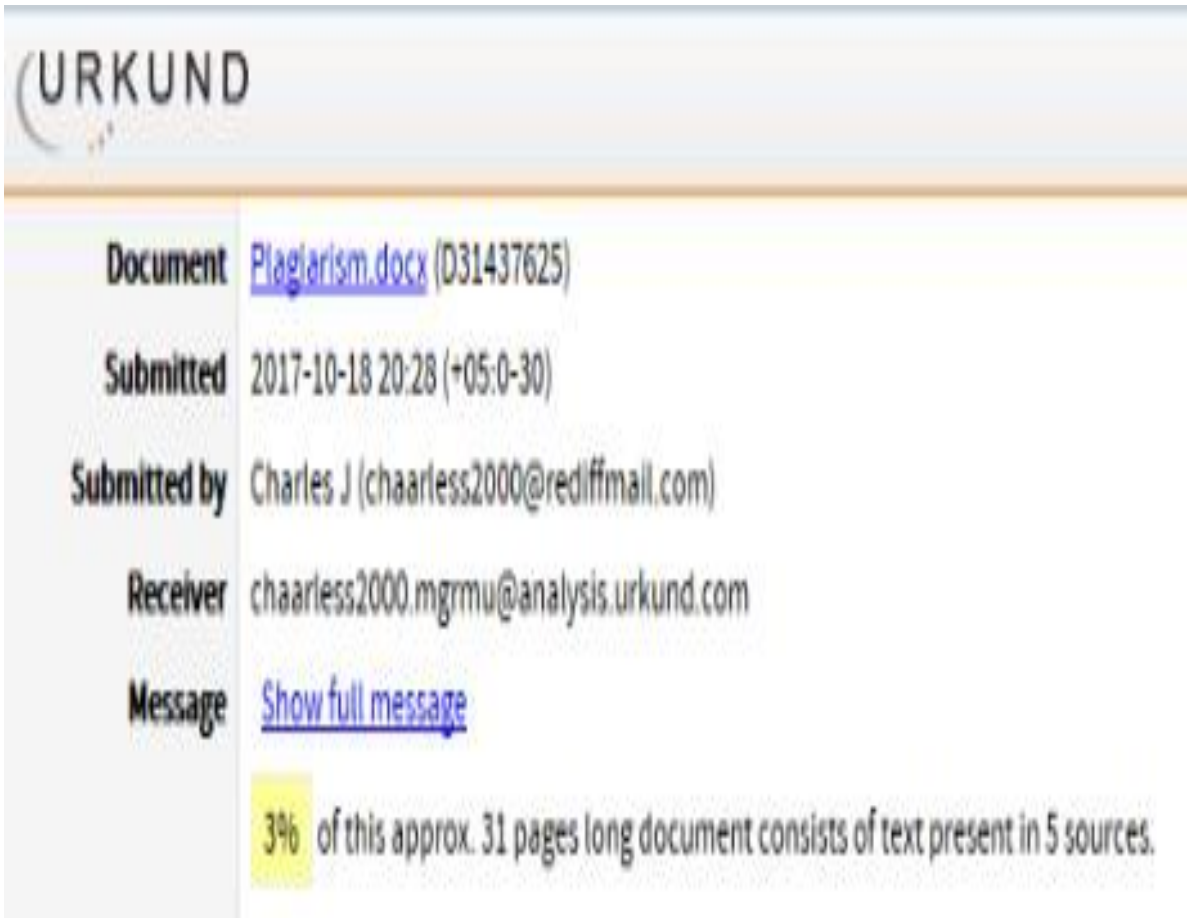

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Contents

AIM:

The aim of this study is to compare the effect of Dexmedetomidine and Lidocaine in preventing cough during emergence from general anaesthesia for thyroidectomy.

OBJECTIVES:

1.Primary Objective:

The primary objective is to compare the effect of Dexmedetomidine and Lidocaine in preventing cough during emergence from general anaesthesia for thyroidectomy.

2.Secondary Objectives:

The secondary objectives are:

a) To compare the effect of Dexmedetomidine and Lidocaine in attenuating haemodynamic responses during emergence from general anaesthesia for thyroidectomy.

b) To compare the effect of Dexmedetomidine and Lidocaine on time taken to awaken from general anaesthesia for thyroidectomy.

INTRODUCTION:

Postoperative neck haematoma requiring emergent surgical evacuation is a rare but dreaded complication of thyroidectomy as the mortality rate is high. Bleeding frequently occurs in the case of sudden violent cough, sneeze or vomit, especially during extubation. So, it is reasonable to take measures to prevent cough during emergence from general anaesthesia, so as to prevent the possible life threatening complication of post thyroidectomy neck haematoma causing airway compromise and possibly, death. Dexmedetomidine has been successfully used to attenuate the haemodynamic responses to tracheal intubation and extubation, in doses ranging between 0.5 mcg/kg to 1 mcg/kg. Lidocaine has also been used in doses between 1 mg/kg to 2 mg/kg to prevent cough during emergence from general anaesthesia. Studies are not available till date comparing these drugs in preventing cough in thyroidectomy. The purpose of this study is to compare the effect of Dexmedetomidine and Lidocaine in preventing cough during emergence from general anaesthesia for thyroidectomy

LITERATURE REVIEW:

General Anaesthesia:

General anaesthesia (1) can be broadly defined as a state of reversible depression of the central nervous system induced by drugs resulting in the loss of response to and perception of any external stimuli. The components of such an anaesthetic state include amnesia, unconsciousness, immobility, analgesia and attenuation of autonomic responses to any noxious stimulation.

In deep plane of anaesthesia, the patency of airway can be compromised. Securing and maintaining the patency of the airway is essential in such a state of anaesthesia. Endotracheal tube, supra-glottic airway device can be used to secure airway and maintain ventilation. Endotracheal intubation was described first as early as in 1788 as a means of resuscitation of the collapsed patient ("apparent dead"), but it was not used for the delivery of anaesthesia until almost for the next 100 years. Placement of endotracheal tube not only secures the airway but also allows delivery of anaesthetic gases for maintenance of anaesthesia throughout the surgery.

Cough:

Cough is a very important protective reflex that occurs via the stimulation of a composite reflex arc. It increases clearance of secretions and particulate matter from the airways and protects the airway from aspiration of foreign body occurring as a result of aspiration or inhalation of particulate substance, pathogens, secretions, postnasal drip, inflammation, and mediators associated with inflammation.

Under normal circumstances coughing serves an important defensive role in the airways and lungs. (2). The cough reflex is initiated by the irritation of cough receptors which are found in the trachea, main carina, branching points of large airways, and more distal smaller airways, also the pharynx. Tracheal, bronchial and laryngeal receptors respond to both chemical and mechanical stimuli. Chemical receptors which are sensitive to heat, acid, and capsaicin-like compounds trigger the cough reflex via activation of the type 1 vanilloid (capsaicin) receptor. Additionally, more such airway receptors are located in the eardrums, external auditory canal, pharynx, paranasal sinuses, pleura, diaphragm, stomach and pericardium. These are likely to be mechanical receptors only, which can be stimulated by triggers such as displacement or touch. (3) (4).

Impulses from stimulated cough receptors traverse an afferent pathway via the vagus nerve to the cough centre in the medulla oblongata, which itself may be under some control by higher cortical centres. The cough centre generates an efferent signal that travels down the vagus, phrenic, and spinal motor nerves to expiratory musculature to produce the cough.

The **cough reflex arc** is constituted by: (2)

1. **Afferent pathway:** Sensory nerve fibres which are branches of the vagus nerve, located in the ciliated epithelium of the upper airways (auricular, pulmonary, superior laryngeal, pharyngeal, gastric) and oesophageal, and cardiac branches from the diaphragm. The afferent impulses go to medulla oblongata diffusely.

2**. Central Pathway (cough centre):** a central co-ordinating region for cough is present in the upper brain stem and the pons.

3. **Efferent pathway:** Impulses from the cough centre travel via the vagus, phrenic, and spinal motor nerves to diaphragm, abdominal wall and muscles. The nucleus retro-ambigualis, by phrenic and other spinal motor nerves, sends impulses to the expiratory and inspiratory muscles; and the nucleus ambiguus, by the laryngeal branches of the vagus to the larynx.

The observation that women are more likely to develop chronic cough than men explains the sex-related differences in cough reflex sensitivity. (5) (6).

The mechanical events of cough can be categorised into three phases (7) :

1. Inspiratory phase: Inhalation, which generates the volume required for an effective cough.

2. Compression phase: Closure of the larynx combined with contraction of diaphragm, muscles of abdominal wall, and chest wall result in a swift rise in intra-thoracic pressure.

3. Expiratory phase: The glottis opens, which results in high expiratory airflow and the coughing sound. Compression of large airway occurs. Mucus from the airways is dislodged by the high flows, which also allows removal of mucus from the trachea-bronchial tree.

During vigorous coughing, intra-thoracic pressures can reach up to 300 mm Hg and expiratory velocities may reach up to 800 kilometre per hour. (8). These velocities and pressures are responsible for the beneficial effects of cough on mucus clearance.

Also, they are responsible for numerous other complications of cough, including self-consciousness, exhaustion, headache, insomnia, hoarseness, musculoskeletal pain, dizziness, urinary incontinence and excessive perspiration. (9). Stimulation of the larynx produces a choking type of cough which is not preceded by inspiration. Inadequate muco-ciliary clearance mechanisms (as in cystic fibrosis or bronchiectasis) may produce a pattern of coughing with less violent acceleration of air and a sequence of interrupted expirations without any intervening inspiration. (2).

Cough in Tracheal Extubation:

Tracheal extubation can be performed while either patients are under deep anaesthesia or when they are awake. Each technique has its own pros and cons. (10) (11). Extubation in a light plane of anaesthesia is the most important concern in awake extubation. While extubation in deep plane of anaesthesia may leave the patient with an unprotected airway. Deep extubation might prevent the problem of cough and straining, (10) as opposed to awake extubation, and avoid the possibilities of laryngospasm and oxygen desaturation. (10) (11). Nonetheless, deep extubation technique has the potential of exposing the patients to the risk of airway obstruction or aspiration as it prolongs the time interval between tracheal extubation and return of protective airway reflexes, which is always a great concern after general anaesthesia. Wakefulness is determined by the return of pharyngeal or laryngeal reflexes, eye

opening, grimacing, coughing, and purposeful movement, and in this situation, the patients are in full control of their airway reflexes and can maintain adequate ventilation. (10) (11).

Events such as aspiration, laryngospasm, inadequate ventilatory drive or airway obstruction can result in hypoxaemia. Such hypoxaemia can usually be corrected immediately. Occasionally, post-extubation hypoxaemia can progress quickly, and if uncorrected, can result in very serious complications like brain damage and death. (12).

Coughing is a common clinical problem in most patients during emergence from general anaesthesia in the presence of a tracheal tube. (13). Apart from respiratory and airway related events, emergence from general anaesthesia can result in a number of undesirable side effects including hypertension, tachycardia and agitation. These side effects may cause haemorrhage from the surgical wound site and also increase the in intraocular and intracranial pressures. (14).

Administration of opioids or local anaesthetics, and extubation in a deeper plane of anaesthesia have been suggested to prevent such adverse emergence events. (11) (15) (16). The administration of opioids before emergence may be beneficial for preventing agitation, cough and haemodynamic response but, it may cause unpredictable and undesirable delayed emergence. (16).

In paranasal sinus and nasal operations, smooth emergence from general anaesthesia is desirable because bucking and coughing during awakening very often

stimulate the oozing of blood, which may further lead to more airway stimulation and subsequently to more coughing and bucking. (10).

The incidence of coughing during emergence from general anaesthesia in the presence of endotracheal tube has been estimated as ranging between 38 and 96%. (17) (18). Bucking and coughing induced by endotracheal tube can complicate emergence from general anaesthesia. They may possibly be associated with breath-holding which may cause a decrease in oxygen saturation and hypoxaemia (19). Moreover, bucking and coughing can precipitate serious bronchospasm in patients with hyper-reactive airways. (20) (21). They can also precipitate larngospasm post extubation, which can further lead to severe hypoxaemia, brain damage and death.

The tracheal tube and its cuff stimulate the stretch receptors and the rapidly acting irritant receptors in the trachea. (22). Those irritant receptors are thought to be the receptors involved in the cough reflex. (23) (24). Any stimulation such as head turning, oropharyngeal suctioning, pillow removal, and bodily movements can cause tracheal irritation and awakening.

Thyroidectomy:

Thyroidectomy is the procedure of surgical removal of whole or part of the thyroid gland. It is done to treat diseases of the thyroid gland including:

- Large goitres or thyroid nodules causing symptomatic obstruction
- Hyperthyroidism
- Thyroid cancer

- Multi-nodular Goitre

Thyroid surgery (25) was performed well before the physiology of thyroid gland was understood. The procedures were often fraught with complications, including infection, massive haemorrhage and injury to adjacent structures in the neck, all of which were associated with morbidity and mortality rates of as high as 40%. With the advent of aseptic technique and improvement in technology, mortalities and morbidities associated with these surgeries decreased.

Post-Thyroidectomy Neck Haematoma:

Nowadays, thyroidectomy, compared to olden days, is a relatively safe surgical procedure for treating several diseases of the thyroid gland compared with conservative methods. The common indications for thyroidectomy are the presence of thyroid nodules, multinodular goitres and thyroid carcinoma. The thyroid gland is an organ with high blood flow and is second only to the adrenal glands in terms of relative vascular perfused organ in the body (26). Post-operative bleeding, therefore, may be a complication of thyroid surgery. The reported incidence of post-thyroidectomy bleeding varies between approximately 0.05 and 1.25 percent, but depending on patient and surgeon factors (like experience of the surgeon, number of thyroidectomy done), it can be up to 4 percent. (27) (28). The incidence of post thyroidectomy bleeding is 1.36% in most centres, of which re-exploration was required in about 0.3%. (29). Shelby H et al (29) reported that, during a 40-year period during which 10,201 thyroidectomies were performed at the Royal North Shore Hospital, 1.2% required re-operation for haemorrhage.

Generally, the risk of post thyroidectomy bleeding mainly depends on the extent of the operation, patient factors (such as size of tumour, male gender, older age) and the experience of the operating surgeons (28) (27). Although rare, the post-thyroidectomy bleeding may be life-threatening. Although some hematomas present superficially, in severe cases, cervical hematomas can compress the airway, necessitating surgical evacuation or tracheostomy in about 4.8% of patients. (30) (31) (32) (33). Death has occurred from cardiac arrest and respiratory distress. (34) (35). Occasionally, the haemorrhage also necessitates blood transfusions, 7.1%. (30) (31) (27). Mortality is about three times more likely in patients who had hematoma. Postoperative haemorrhage has been attributed to three categories of risk: surgical technique, patient predisposition, and thyroid pathology. (36). Smokers have a recognized increased bleeding tendency. (38) (36). Most bleeding after thyroidectomy is due to higher systolic blood pressures in the immediate post-operative period. (38). Higher systolic blood pressures postoperatively in excess of 150 mmHg has been associated with an increased risk of haemorrhage after thyroid surgery. (37). Graves' disease and hyperthyroidism were found to be independent risk factors for post-thyroidectomy bleeding. (37). Neck lymph node dissection is an independent predictor for post-thyroidectomy bleeding. (37). Patients who need neck dissection had malignant pathological diagnosis and underwent a large thyroid tissue removal, led to a larger dead space and allowed a hematoma to form easily. Neck dissection requiring greater extent of dissection is more likely to damage the surrounding tissue, such as infra-hyoid muscles or jugular vein. Bleeding frequently occurred after sudden violent cough, sneeze or vomiting often during immediate post-operative period.(37). Violent

cough or vomit and unexpected hypertension were also responsible for the subcutaneous tissue bleeding. (37). On sudden violent cough, sneeze or vomit, the upper pole would lift with thyroid cartilage, generating forces between the upper pole and cricothyroid, making the part cricothyroid evulsion, loosing bleeding ligation, and lead to the bleeding after operation. (37).

Methods to Prevent Cough during Extubation:

Several strategies have been tried to minimise or prevent cough during emergence from general anaesthesia in the presence of tracheal tube. The strategy can be the extubation technique or a pharmacological intervention to prevent coughing during emergence from general anaesthesia.

Extubation in deep plane of anaesthesia has been advocated to obtund the laryngeal reflexes. (39) . This technique offers the advantage of a smooth extubation with minimal airway stimulation, thereby preventing cardiovascular stimulation and subsequent haemodynamic response, reducing coughing, and reducing intracranial, intraocular, and middle ear pressure changes. Removal of the tracheal tube while patients remain deeply anesthetised may be advantageous in various situations (10).

Intravenous lidocaine is widely used to prevent haemodynamic and airway reflexes during extubation but the duration of action is short. (40). Lidocaine alkalinised with 8.4% sodium bicarbonate has been used to prevent cough during emergence from general anaesthesia. (41). Alkalinised Lidocaine instilled through the endotracheal tube suppressed cough if given approximately 5 min before extubation, and found it to be superior to intravenous injection given 3 min before extubation. (42).

Low dose remifentanil has been used to conduct a smooth extubation. (43). Alfentanil has also been used to suppress cough and agitation during emergence from general anaesthesia. (16). The administration of opioids before emergence may be beneficial for preventing cough, agitation, and hemodynamic response but, it may cause unpredictable delayed emergence. (16).

Haemodynamic Responses during Emergence from General Anaesthesia:

Emergence from anesthesia and tracheal extubation are usually associated with tachycardia, hypertension and high plasma catecholamine levels. (44). These responses may lead to post-operative haemorhage, pulmonary oedema, cerebrovascular haemorrhage and cardiac failure. (45). Various drug regimens and techniques have been used from time to time for attenuating the stress response to laryngoscopy and intubation, including opioids, barbiturates, benzodiazepines, beta blockers, calcium channel blockers, dexmedetomidine, lidocaine, vasodilators, or by extubation under deep anesthesia. (46) (21) (47) (48) (49) (50) (51) (52) (53).

Recovery from Anaesthesia:

Recovery from anaesthesia may be defined as a state of consciousness of an individual when the person is awake or easily aroused and aware of his surroundings and identity. (54) (55). Awakening results from elimination of anaesthetic agents from the brain. Patients usually respond to verbal stimuli when alveolar anaesthetic concentration is decreased to about 30% of minimum alveolar concentration (MAC) (MAC awake) if unimpeded by other factors. (55). Recovery from intravenous opioids and hypnotics may be more variable and difficult to quantify than recovery from inhalational and neuromuscular blocking agents. Patients should not leave the

operating room or the post-anaesthesia care unit unless they have a patent airway, stable hemodynamic parameters, adequate ventilation and oxygenation. Irrespective of age or American Society of Anaesthesiologist physical status category, higher incidence of early postoperative respiratory complications is noted when the patient is transferred to post anaesthesia care unit in an unresponsive state. (56).

The entire process of recovery after anaesthesia can be divided into three phases.

1.Immediate recovery - consists of recovery of protective airway reflexes, return of consciousness and resumption of motor activity. This stage usually lasts for a short time.

2. Intermediate recovery - the patient regains his power of coordination and the feeling of dizziness disappears. This stage usually lasts for one hour after short anaesthetic. Outpatient may be considered fit for discharge with a responsible escort.

3. Long-term recovery - full recovery of coordination and higher intellectual function. It may last for hours or even days. (56) (57). Patients cannot be considered fully recovered until they have returned to their preoperative physiological state. (54).

Abnormally slow pace of regaining consciousness after general anaesthesia is characterised by persistent somnolence. It is defined as a state of unresponsiveness from which the patient cannot be aroused. In otherwise healthy patients who have undergone short operative procedures, delayed recovery is usually secondary to some underlying undiagnosed condition or medical error. (54). Even after prolonged

anaesthesia, a response to stimulation should occur between 60 and 90 minutes. (54) (58). The incidence of unresponsiveness between 15 and 90 min after general anaesthesia among mixed surgical patients is about 9%. (30) Dissociative coma, thyroid failure, myxoedema coma, hunter syndrome (mucopolysaccharide storage disease), drug abuse, valproate toxicity and lidocaine infusion for arrhythmias are some rare causes of delayed recovery. (54) (55).

Risk Factors for Delayed Awakening:

Table 0.0 (55)

Patient factors	Drug factors	Surgical and anesthetic factors	Metabolic factors
Extremes of age	Dosage	Long surgery and anesthesia	Hypo/hyperglycemia
Gender	Time of administration	Muscle relaxant use	Hypo/hypernatremia
Genetic variation	Blood gas solubility	Hypotension	Hypothermia
Co-morbidities	Metabolism	Hypoxia	Hypothyroidism
Body habitus	Excretion	Embolism	Hepatic and/or renal failure
Cognitive dysfunction	Drug interactions	Cardiac/neurosurgery	Central anticholinergic syndrome
Seizures	Fluid overload	Regional techniques with sedation	Acidosis
Stroke	Local anesthetic toxicity	Painful stimulation	Coagulation defects

Dexmedetomidine: (1) (58) (59)

Dexmedetomidine is a highly selective, specific, and potent alpha adrenergic agonist (1,620:1 alpha2 to alpha1). This drug is the dextroisomer and pharmacologically active component of medetomidine, which has been used for many years in veterinary practice for its hypnotic, sedative, and analgesic effects. Compared with clonidine, Dexmedetomidine is seven to ten times more selective for alpha2

receptors and has a shorter duration of action than clonidine. In this regard, Dexmedetomidine is considered a full agonist at the alpha2 receptor, whereas clonidine is a partial agonist (ratio of alpha2 to alpha1 activity for clonidine is 220:1). Atipamezole is a specific and selective alpha2 receptor antagonist that rapidly and effectively reverses the sedative and cardiovascular effects of intravenous Dexmedetomidine. The elimination half time of Dexmedetomidine is 2 to 3 hours compared with 6 to 10 hours for c1onidine. Dexmedetomidine is highly protein bound (>90%) and undergoes extensive hepatic metabolism. The resulting methyl and glucuronide conjugates are excreted by the kidneys. Dexmedetomidine has weak inhibiting effects on cytochrome P450 enzyme systems that might manifest as increased plasma concentrations of opioids as administered during anaesthesia. As with clonidine, pre-treatment with Dexmedetomidine attenuates hemodynamic responses to tracheal intubation, decreases plasma catecholamine concentrations during anaesthesia, decreases peri-operative requirements for inhaled anaesthetics and opioids, and increases the likelihood of hypotension. Dexmedetomidine decreases MAC for volatile anaesthetics in animals by > 90% compared with a plateau effect between 25% to 40% for clonidine.

In patients, isoflurane MAC was decreased 35% and 48% by Dexmedetomidine plasma concentrations of 0.3 ng/mL and 0.6 ng/mL, respectively. Despite marked dose-dependent analgesia and sedation produced by this drug, there is only mild depression of ventilation. Dexmedetomidine in high doses (loading dose of 1 mcg/kg intravenous followed by 5 to 10 mcg/kg/hour intravenous) produces total intravenous anaesthesia without associated depression of ventilation. The preservation

of breathing provides a potential anaesthetic technique for patients with a difficult upper airway. As with c1onidine, Dexmedetomidine has been reported to be effective in attenuating the cardio-stimulatory and post-anaesthetic delirium effects of ketamine. Addition of 0.5 mcg/ kg Dexmedetomidine to lidocaine being administered to produce intravenous regional anaesthesia improves the quality of anaesthesia and postoperative analgesia without causing side effects. Dexmedetomidine increases the range of temperatures without triggering thermoregulatory defenses. Dexmedetomidine, like clonidine, is likely to promote perioperative hypothermia and also prove to be an effective treatment for shivering. Severe bradycardia may follow the administration of Dexmedetomidine and cardiac arrest has been reported in a patient receiving a Dexmedetomidine infusion as a supplement to general anaesthesia Dexmedetomidine (0.2 to 0.7 mcg/ kg/ hour intravenous) is useful for sedation of postoperative critical care patients in an intensive care unit environment, particularly when mechanical ventilation via a tracheal tube is necessary. In comparison with remifentanil, Dexmedetomidine infusions do not result in clinically significant depression of ventilation and sedation exhibits some similarity with natural sleep. Following tracheal extubation, Dexmedetomidine-sedated patients breathe spontaneously and appear calm and relaxed. Both clonidine and Dexmedetomidine are useful in the intensive care unit to prevent drug withdrawal symptoms following long-term sedation with benzodiazepines. Its sympatholytic and vagomimetic actions can cause systemic hypotension and bradycardia. The ability to specifically antagonize the sedative effects of Dexmedetomidine with atipamezole may be useful.

Lidocaine: (1) (58) (59)

Lidocaine was synthesized as an amide local anaesthetic by Lofgren in 1943. Lidocaine is effective topically and is a highly efficacious cardiac antidysrhythmic drug. Lidocaine prevents transmission of nerve impulses (conduction blockade) by inhibiting passage of sodium ions through ion-selective sodium channels in nerve membranes. In addition to sodium ion channels, local anaesthetics block voltage-dependent potassium ion channels. Considering the similarity in structure between voltage-dependent calcium ion channels and sodium ion channels, it is quite possible that calcium ion currents (L-type most sensitive) may also be blocked by local anaesthetics. Although all local anaesthetics are considered primarily ion channel blockers, there is also considerable evidence that these drugs may also act on G-protein coupled receptors. Local anaesthetics can be used to produce topical anaesthesia by placement on the mucous membranes of the nose, mouth, tracheobronchial tree, oesophagus, or genitourinary tract. Lidocaine 2% to 4% is most often used. The inhalation of local anaesthetics by normal subjects does not alter airway resistance and may even produce mild bronchodilation. In contrast, inhalation of nebulized lidocaine can cause bronchoconstriction in some patients with asthma, which may become an important consideration when bronchoscopy is planned in these patients. The intravenous injection of a local anaesthetic solution into an extremity isolated from the rest of the systemic circulation by a tourniquet produces a rapid onset of anaesthesia and skeletal muscle relaxation. The duration of anaesthesia is not dependent on the specific local anaesthetic, and it is determined by how long the tourniquet is kept inflated. The mechanism of action by which local anaesthetics

produce intravenous regional anaesthesia is not clearly known, but it probably reflects the action of the local anaesthetic on nerve endings as well as nerve trunks.

Lidocaine is the most frequently selected amide local anaesthetic for producing this type of regional anaesthesia. Apart from suppressing ventricular cardiac dysrhythmias, the intravenous administration of lidocaine may also increase the defibrillation threshold.

The principal metabolic pathway of lidocaine is oxidative dealkylation in the liver to monoethylglycinexylidide followed by hydro lysis of this metabolite to xylidide. Monoethylglycinexylidide has approximately 80% of the activity of lidocaine for protecting against cardiac dysrhythmias in animal models. The elimination half-time of this metabolite is long, which account for its efficacy in controlling cardiac dysrhythmias after the infusion of lidocaine is discontinued. Xylidide exhibits only about 10% of the cardiac anti-dysrhythmic activity of lidocaine. In humans, approximately 75% of xylidide is excreted in the urine as 4-hydroxy-2,6-dimethylaniline. Decreased in hepatic blood flow which may occur under anaesthesia and hepatic diseases, can decrease the rate of metabolism of lidocaine. For instance, compared with normal patients, the elimination half-time of lidocaine is increased more than fivefold in patients with liver dysfunction. When patients are anesthetised with volatile anaesthetics, decreased hepatic metabolism of lidocaine should be anticipated, as hepatic blood flow can be decreased. In the presence of pregnancy induced hypertension, maternal clearance of lidocaine is prolonged due to decreased hepatic blood flow or HELLP syndrome where there can be hepatic necrosis and subsequent impaired hepatic function. Hence, repeated administration of

lidocaine can result in higher plasma concentrations than in normotensive pregnant women.

The principal side effects related to the use of lidocaine are allergic reactions and systemic toxicity due to excessive plasma and tissue concentrations. Systemic toxicity is estimated to result in seizures in 1 to 4 per 1,000 patient exposures.

Lidocaine has also been observed to suppress cough reflex when used as supplement of general anaesthesia. Although the mechanism by which intravenous lidocaine suppresses respiratory and laryngeal reflex responses is largely unknown, possible effects may include general anaesthesia, depression of motor function and direct blockade of noxious stimuli (60). Lidocaine may cause suppression of cough by causing depression of brain stem functions. Lidocaine may also act by anaesthetising cough receptors in the hypopharynx and trachea. (61). Administration of intravenous lidocaine may suppress chemically and mechanically induced airway reflexes, including cough reflex. (61).

Justification for the Study:

Qing Fan et al (43) studied Dexmedetomidine and Remifentanil in preventing cough during extubation in patients undergoing ear surgeries. This study included 75 patients (25 patients in each arm) in the age group between 20 and 60 years undergoing elective middle ear surgery. The patients were randomised into three arms. Patients in one arm received Remifentanil 0.03 mcg/kg/minute infusion over 10 minutes, patients in the second arm received Dexmedetomidine 0.5 mcg/kg infusion over 10 minutes and patients in the third arm received Dexmedetomidine 0.7 mcg/kg infusion over 10 minutes. Smooth extubation without cough was achieved in 22/25

(88%) patients in Remifentanil arm, 15/25 (62.5%) patients in 0.5 mcg/kg Dexmedetomidine arm, 22/25 (88%) patients in 0.7 mcg/kg Dexmedetomidine arm. There was also less incidence of post-operative nausea and vomiting in both the Dexmedetomidine arms. There was no significant difference in time taken for awakening between all three arms. This study concluded that both Remifentanil and Dexmedetomidine at 0.7 mcg/kg are effective in preventing cough during extubation. So, Dexmedetomidine produced a dose-dependent effect in providing smooth extubation without significantly prolonging the recovery from anaesthesia. Compared to remifentanil, the benefits of dexmedetomidine included hemodynamic stability, opioid sparing, and less post-operative nausea and vomiting. The disadvantages of dexmedetomidine included lower tidal volume and blood pressure.

Intravenous Lidocaine was found to suppress the cough reflex produced by moving the endotracheal tube. (62). A test dose of 2% lidocaine, 40 mg, followed by an additional 150-200 mg injected in less than 60 seconds suppressed the cough reflex successfully for 8-9 min during bronchography after tracheal intubation. (63).

Yukioka H et al (64) studied different doses of Lidocaine in suppressing cough during extubation in patients in the age group between 15 and 55 years, undergoing orthopaedic, urologic, gynaecologic and general surgeries. One hundred patients were randomised in to five arms, with doses of 0.5, 1.0, 1.5 and 2.0 mg/kg Lidocaine and placebo (normal saline). The incidence of coughing was 70% in the placebo arm, 65% with 0.5 mg/kg Lidocaine, 30% with 1.0 mg/kg Lidocaine, 20% with 1.5 mg/kg Lidocaine and 0% with 2.0 mg/kg Lidocaine. The incidence of coughing decreased as the dose of intravenous lidocaine increased. It concluded that the optimal dose of

Lidocaine to suppress cough during extubation is 2 mg/kg with no serious adverse effects. There was no significant difference in side effects between the different dose arms of Lidocaine. Lidocaine has been used in doses between 1 mg/kg to 2 mg/kg as intravenous bolus to prevent cough during emergence from general anaesthesia with variable results. (64) (65).

Ashraf MA Moustafa et al (53) compared the efficacy of the Dexmedetomidine-Lidocaine combination with each drug alone in suppressing the hemodynamic and catecholamine stress responses during tracheal extubation and emergence from general anesthesia. in elective orthopaedic surgeries. Sixty hypertensive patients (ASA II–III), defined as systolic blood pressure more than 160 mm Hg and/or diastolic blood pressure more than 95 mmHg, undergoing elective orthopaedic surgery were assigned to a randomized in to three arms, with double-blind approach. One arm received Dexmedetomidine 0.1 mcg/kg, the second arm received Lidocaine 1 mg/kg, and the third arm received Dexmedetomidine and Lidocaine combination with same dose with 20 patients in each arm. Incidence of cough was secondary outcome in this study. Smooth extubation without cough or with minimal cough was achieved in 15/20 (75%) patients in Lidocaine arm, 6/20 (30%) patients in Dexmedetomidine arm, 15/20 (75%) patients in combination arm. It was found that HR and MAP increased temporarily after tracheal extubation in patients receiving Lidocaine. However, these hemodynamic changes were completely inhibited in those receiving Dexmedetomidine plus Lidocaine, but suppressed to some extent with Dexmedetomidine alone. It concluded that Lidocaine was better in preventing cough

during extubation, and Dexmedetomidine was better in suppressing haemodynamic responses during extubation.

The effect of lidocaine on the hemodynamic changes may be because of its direct cardiac depression and peripheral vasodilation as it could significantly depress all excitable membranes including the heart. (66). It may also act through inhibition of cough or strain associated with tracheal extubation that could cause hypertension and tachycardia. (67). Attenuation of the activity in afferent C fibers from the larynx may contribute toward this beneficial effect. (68). In addition, lidocaine may act centrally to increase the depth of anaesthesia. (69).

Sharma VB, Prabhakar H et al (65) studied Dexmedetomidine and Lidocaine in preventing airway and haemodynamic responses during extubation in patients undergoing elective spine surgeries. This study included 60 patients, randomised in to three arms, with 20 patients in each arm. One arm received Dexmedetomidine 0.5 mcg/kg, the second arm received Lidocaine 1.5 mg/kg, and the third arm received normal saline (placebo). Cough was graded from grade 1 to grade 5, with grade 1 being no cough, grade 2 minimal cough (one or two attempts at coughing), grade 3 moderate cough (three or four attempts at coughing), grade 4 heavy coughing (5 or more attempts at coughing) and grade 5 severe cough (laryngospasm, no breathing). 16/20 (80%) had no cough in the Dexmedetomidine arm, whereas the rest 4/20 (20%) had grade 2 cough (mild cough). 13/20 (65%) patients had no cough in the Lidocaine arm, whereas, 7/20 (35%) had grade 2 cough (mild cough). 7/20 (35%) patients had no cough in the placebo group, whereas, 11/20 (55%) had grade 2 cough (mild cough), and 2/20 (10%) had grade 3 cough (moderate cough). The heart rate increased

in all the groups but the increase was more in patients in Lidocaine group than in Dexmedetomidine group. Only one patient had bradycardia in the Dexmedetomidine group. The MAP increased for the initial 3 minutes of drug administration in Dexmedetomidine group. However, Dexmedetomidine attenuated the increase in blood pressure to a greater degree than Lidocaine. The airway response was better attenuated with Dexmedetomidine than with Lidocaine. The need for postoperative analgesia was delayed after administration of Dexmedetomidine. It concluded that both Lidocaine and Dexmedetomidine were comparable in attenuating haemodynamic response, Dexmedetomidine was better in attenuating airway response, and there was no difference in time taken for emergence.

Coughing may potentially trigger post thyroidectomy bleeding by causing slipping of ligatures and disruption in the haemostasis. It can significantly increase the mortality and morbidity. Hence it is reasonable to take measures to prevent coughing during emergence from general anaesthesia after thryroidectomy. Both Dexmedtomidine and Lidocaine have been shown to decrease the occurrence of cough during tracheal extubation in various studies, but there is no study comparing these drugs in preventing cough during emergence from general anaesthesia after thyroidectomy. Also it is not a standard of care to administer either of these drugs during emergence from general anaesthesia after thyroidectomy. Hence, the purpose of this study is to determine whether the administration of Dexmedetomide or Lidocaine will minimise or prevent coughing during extubation in thyroidectomy, and to compare their effects.

NULL HYPOSTHESIS:

There is no difference between the effect of Dexmedetomidine and Lidocaine in preventing or minimising cough during emergence from general anaesthesia after thyroidectomy.

STUDY DESIGN:

This is a double-blinded randomised control trial, with Dexmedetomidine in one arm and Lidocaine in the other arm.

METHODS:

The study proposal was submitted the Institutional Review Board (IRB), also including the Ethics Committee. After approval from the IRB, the study was registered in Clinical Trials Registry of India. Recruitment and data collection was started on 29th March 2017, and ended on 10th August 2017.

Inclusion Criteria:

1. All Adult Patients (Age ≥ 18)
2. ASA I, II, III
3. Patients undergoing Thyroidectomy
4. Patients given Consent

Exclusion Criteria:

1. Known Hypersensitivity to Dexmedetomidine or Lidocaine
2. Baseline Heart Rate < 60/minute
3. Uncontrolled Systemic Hypertension
4. URTI / LRTI within 2 weeks

5. Patients on Anti-arrhythmic Drugs
6. Patients on Beta Blocker Drugs

Intervention and Comparator Agents:

Intervention Agent 1 – Dexmedetomidine (Intervention Agent)

Intervention Agent 2 – Lidocaine (Comparator Agent)

To compare intervention agents 1 and 2.

Method of Randomisation:

The patients were randomised in to one of two groups by computer generated block randomisation in blocks of 4.

Method of Allocation Concealment:

Sequentially numbered, sealed, opaque envelopes were used, and they were opened only in the operation theatre after the patient is anaesthetised.

Blinding and Masking:

It is a double blinded study as the participant and outcome assessors were blinded to treatment allocation. Masking was employed to prevent observer bias. An anaesthesiology technologist, not involved in the study, opened the envelope and loaded the drugs accordingly, and labelled with only study numbers on the syringes. The treating anaesthesiologist administered the drugs and observed the effect, and he/she was also blinded. As the methods of administration of the two drugs are different, all patients received two injections – one as an infusion over 15 minutes and the other as a bolus. One of them was the study drug and the other was normal saline. This is to blind the treating anaesthesiologist, who is also the observer of the effect.

Primary Outcome:

The primary outcome is occurrence of no cough during emergence and in post anaesthesia care unit (PACU).

Secondary Outcomes:

The secondary outcomes are

1. Haemodynamic response (Heart Rate, Blood Pressure) during emergence and in PACU.

2. Time taken for awakening.

Methodology:

All adult patients over the age of 18, posted for thyroidectomy surgery by the department of Endocrine Surgery, Christian Medical College, Vellore were interviewed. Consent was taken by the primary investigator after explaining the procedure in detail in the ward in the evening prior to the operation. Consented patients were randomized in to two arms, the Dexmedetomidine arm and the Lidocaine arm. The patients underwent the surgery as per routine. All anaesthetic agents and techniques were standardised to eliminate confounding factors. Opaque, sealed envelope were opened outside the operating room, and the drugs were loaded appropriately and labelled with study number by an anaesthesiology technologist not involved in the study or the operation. Thus the treating anaesthesiologist is blinded. Group A received 1 mcg/kg of Dexmedetomidine (infused intravenously over 15 minutes) and normal saline bolus. Group B received 2 mg/kg of Lidocaine (given as intravenous bolus) and normal saline infusion for 15 minutes. Heart rate and blood

pressure were recorded prior to induction, every 5 minutes intra-operatively. Any occurrence of cough during emergence, extubation, in PACU were recorded. Cough was graded as, grade 1 – no cough, grade 2 – mild cough – predominantly breathing, intermittent coughing (1-3 attempts at coughing), grade 3 – moderate cough - intermittent breathing, predominantly coughing (4 or more attempts at coughing), grade 4 - severe cough (laryngospasm, no breathing). Standard protocol was followed for all patients so as to eliminate confounding factors. The standardised protocol used is as follows:

-No sedative premedication on the day prior to surgery or on the day of surgery

- Standard monitors for intraoperative monitoring as per ASA guidelines

- Induction of anaesthesia with Fentanyl 2 mcg/kg, Propofol 2mg/kg, Atracurium 0.5 mg/kg

- No Lidocaine at intubation

- Size 6.5 ETT for female and size 7.0 ETT for male

- ETT cuff pressure measured after intubation, kept between 20 to 30 cm of water

- Dexamethasone 0.1 mg/kg IV after intubation

- Isoflurane for maintenance of anaesthesia – MAC maintained between 0.8 to 1.0

- Analgesia with Paracetamol 15 mg/kg (up to 1 g), Fentanyl up to 5 mcg/kg

- No Morphine / Tramadol / Diclofenac / Regional Analgesia was administered

- Intermittent Atracurium for muscle relaxation as required

- Study drug infusion started when closure of muscle layer started

- The infusion rate set as body weight in ml/hour and stopped in 15 minutes

- Isoflurane stopped when closure of skin started

- Fresh gas flow increased and Reversal of muscle relaxant administered when the skin closure ended

- Study drug bolus given as body weight/10 ml when MAC reached 0.3

- ETT cuff pressure measured at MAC 0.3, kept between 20 to 30 cm of water

- No calling or touching or stimulating the patient in any way

- Patients waited upon to breathe, open eyes / make purposeful movement

- Shoulder roll / head ring not removed until shifting the patient to trolley

- Oral suction given only after the patient awakened and then ETT removed

- Occurrence of cough at extubation, 1 minute from extubation, 3 minutes from extubation, 5 minutes from extubation, 10 minutes from extubation, 15 minutes from extubation, 30 minutes from extubation and in PACU recorded

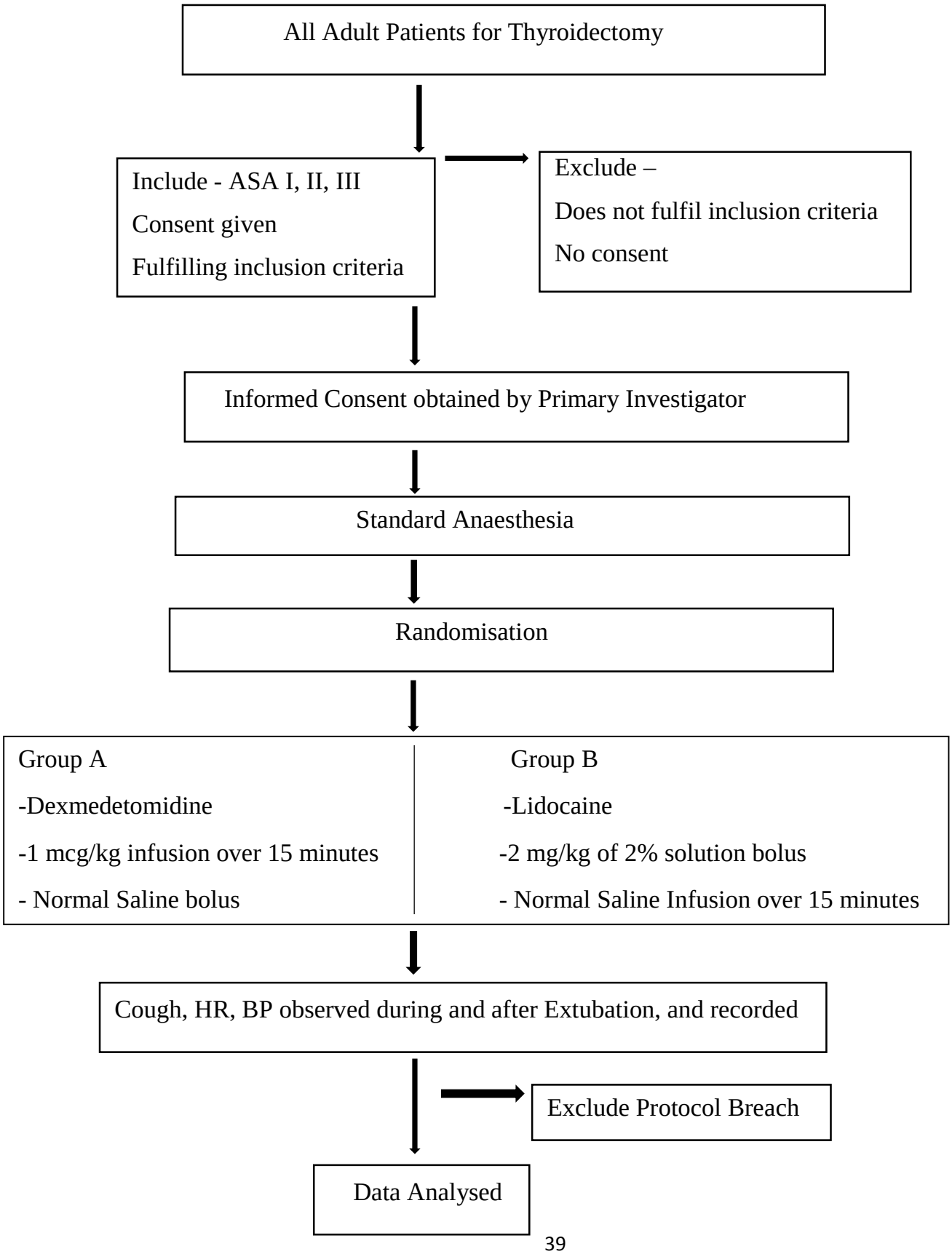
- Haemodynamic responses (heart rate and blood pressure) also recorded at the same time points

- Time taken to awaken calculated from the time of stoppage of isoflurane to the time of extubation

- Data recorded in proforma with all timings

- Grade 3 or grade 4 cough - treated with Propofol

Diagrammatic Algorithm of the Study:



STATSITICAL ANALYSIS:

For the sample size calculation, the statistical input proportion of patients with no cough was taken from the reference article "Comparison of Dexmedetomidine, Lidocaine, and their combination in attenuation of Cardiovascular and Catecholamine responses to Tracheal Extubation and Anaesthesia emergence in Hypertensive Patients" by Ashraf M.A. Moustafa, Hatem Atalla, Hala M. Koptan, Department of Anaesthesia and Intensive Care, Menoufiya University, Egypt, as group I (Dexmedetomidine) & group II (Lidocaine) as 0.10 and 0.35 respectively. The sample size is calculated using Master software version 2.0.

Two Proportion - Hypothesis Testing - Large Proportion - Equal Allocation:

Proportion in Group I	0.1
Proportion in Group II	0.35
Estimated Risk Difference	0.25
Power (1- beta) %	80
Alpha Error (%)	5
1 or 2 sided	2
Required Sample Size for each Arm	43

Formula

$H_o : P_1 = P_2;$ $\quad\quad$ $H_a : P_1 \neq P_2$

$$n = \frac{\left\{ Z_{1-\frac{\alpha}{2}} \sqrt{2\,\bar{P}\,(1-\bar{P})} + Z_{1-\beta} \sqrt{P_1\,(1-P_1) + P_2(1-P_2)} \right\}^2}{(P_1 - P_2)^2}$$

Where,

$$\bar{P} = \frac{P_1 + P_2}{2}$$

P_1 : Proportion in the first group

P_2 : Proportion in the second group

α : Significance level

$1-\beta$: Power

With 80% power, 95% confidence interval and two-sided test, the study required totally 86 patients, 43 patients in each arm. To get more number for the equal allocation, totally 100 patients (Group I = 50: Group II = 50) were planned to be taken for the study to compare the effect of Dexmedetomidine and Lidocaine in preventing cough during emergence from general anaesthesia in patients undergoing thyroidectomy.

A total of 105 patients were interviewed, and after obtaining informed consent, 92 patients were included in the study, as the rest 13 patients did not give consent. Patients were randomised as mentioned before and data were collected. Apart from including the variables for primary and secondary objectives, the data included demographic details, comorbid conditions, anthropometry, allergy, smoking, airway

compression by the thyroid swelling, diagnosis and details of the operation done. Out of the 92 patients, there was protocol breach in 4 patents, hence they were excluded from analysis. Data were entered in Epidata software and analysed using SPSS software.

For continuous data, such as age, the descriptive statistics n, Mean, SD, Median, IQR, Minimum and Maximum were calculated. For categorical data, the number of patients, percentage and proportions were presented. Based on the normality of data, the parametric t test or non-parametric Mann-Whitny test were applied to the data, wherever required. Association between the intervention and outcome was analysed using Chi-Square test. Severity grade of cough were presented as number and percentage and compared. P-values were reported as specified by the statistical software used, at least up to four decimal places. P-values less than 0.0001 were reported as provided by statistical software (e.g. '<0.0001'). All tests were two-sided at α=0.05 level of significance. Difference between two means was assessed using paired t test. Other statistical test was carried out as deemed. All statistical analysis was done using SPSS software version 17.0.

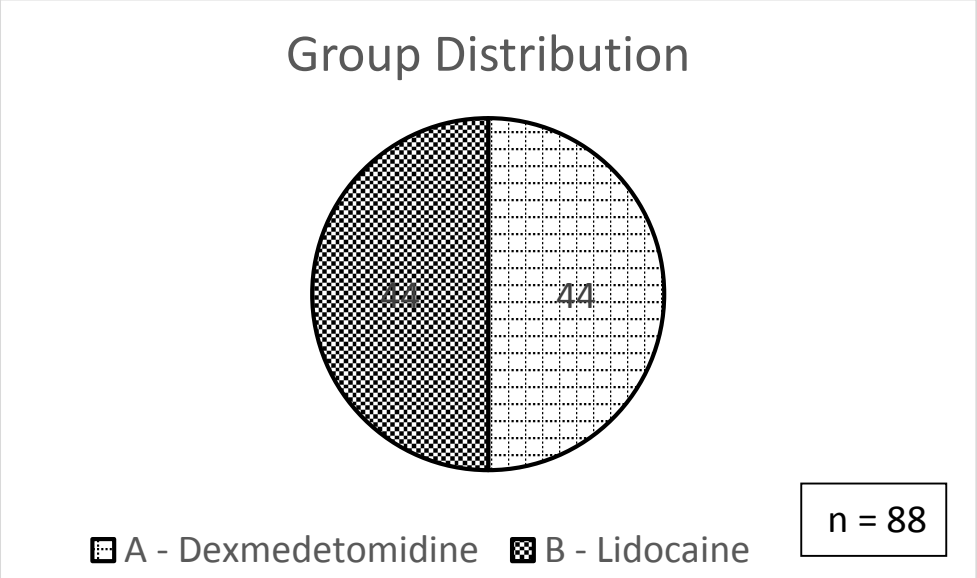
RESULTS:

88 patients in total were analysed, of which 44 belonged to group A (Dexmedetomidine) and 44 belonged to group B (Lidocaine).

Group Distribution:

There were equal number of patients (44 in each) in both groups, hence the number and the percentages during analysis corresponded.

Group	A - Dexmedetomidine	B – Lidocaine
Number of Patients	44	44

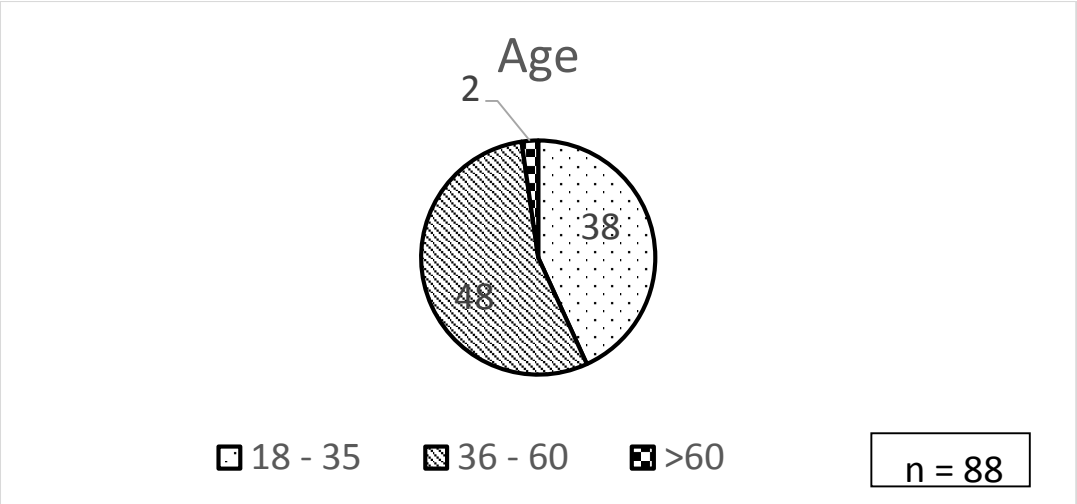


Age Distribution:

38 (43.4%) patients belonged to the age group of 18 to 35 years, 48 (54.2%) patients belonged to the age group of 36 to 60 years, and only 2 (2.3%) patients were above 60 years old. In Dexmedetomidine group, 20 patients belonged to age less than 35 years, 22 patients were between 36 and 60 years and 2 patients were above 60

years. In Lidocaine group 18 patients were less than 35 years, 26 patients were between 36 and 60 years, and no patient was above 60 years.

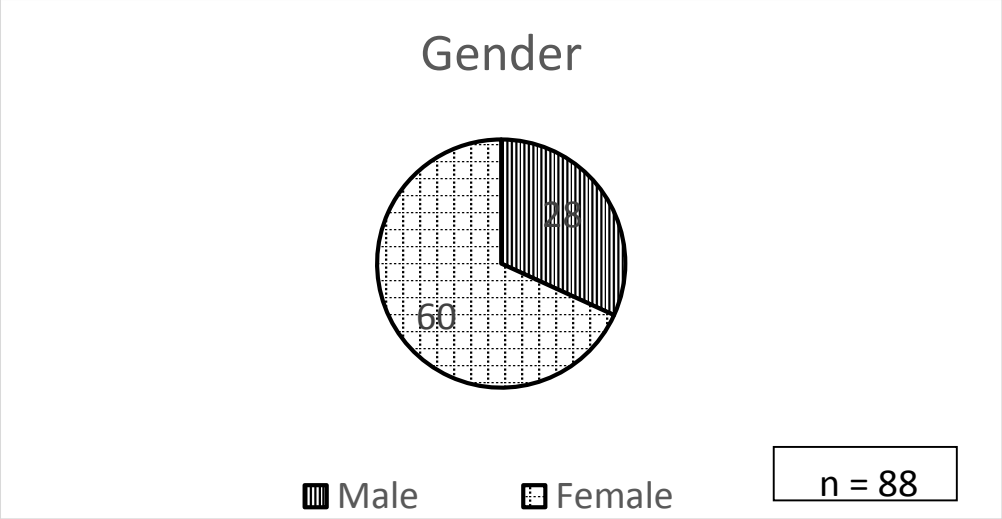
Age	A - Dexmedetomidine	B – Lidocaine
18 – 35 years	20	18
36– 60 years	22	26
>60 years	2	0



Gender Distribution:

28 out of 88 patients were males (31.8%), whereas 60 (68.2%) were females. In Dexmedetomidine group, 15 patients were males and 29 were females. In Lidocaine group, 13 patients were males and 31 were females.

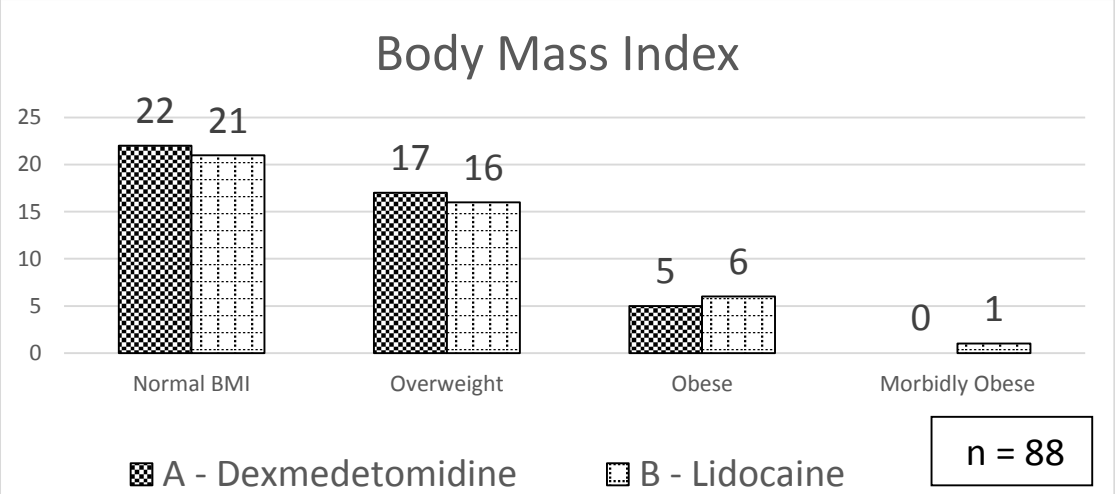
Gender	A - Dexmedetomidine	B - Lidocaine
Male	15	13
Female	29	31



Body Mass Index:

43 patients (48.9%) in total were with normal BMI, 33 patients (37.5%) were overweight, 11 patients (12.5%) were obese, and 1 patient (1.1%) was morbidly obese. In Dexmedetomidne group, 22 patients were with normal BMI, 17 patients were overweight, 5 patients were obese. In Lidocaine group, 21 patients with normal BMI, 16 patients were overweight, 6 patients were obese, and 1 patient was morbidly obese.

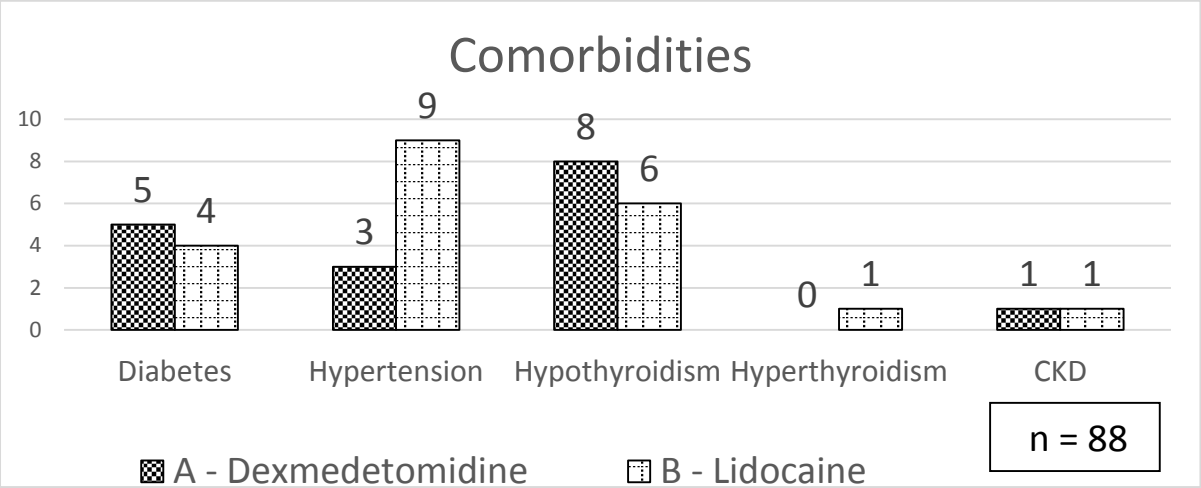
BMI (kg/m^2)	A - Dexmedetomidine	B – Lidocaine
<25	22	21
25.01 – 30	17	16
30.01 - 35	5	6
>35	0	1



Comorbidities:

9 patients had diabetes mellitus (5 in Dexmedetomidine group and 4 in Lidocaine group), 12 patients had hypertension (3 in Dexmedtomidine group and 9 in Lidocaine group), 2 patients had CKD (1 in each group), 1 patient had hyperthyroidism (belonged to Lidocaine group), 14 patients had hypothyroidism (8 in Dexmedetomidine group and 6 in Lidocaine group). 2 patients had bronchial asthma belonging to one group each. The patient in Lidocaine group had grade 2 cough at extubation, and the patient in Dexmedetomidien group had no cough at extubation. One patient had COPD, who was in Lidocaine group, had grade 2 cough at extubation.

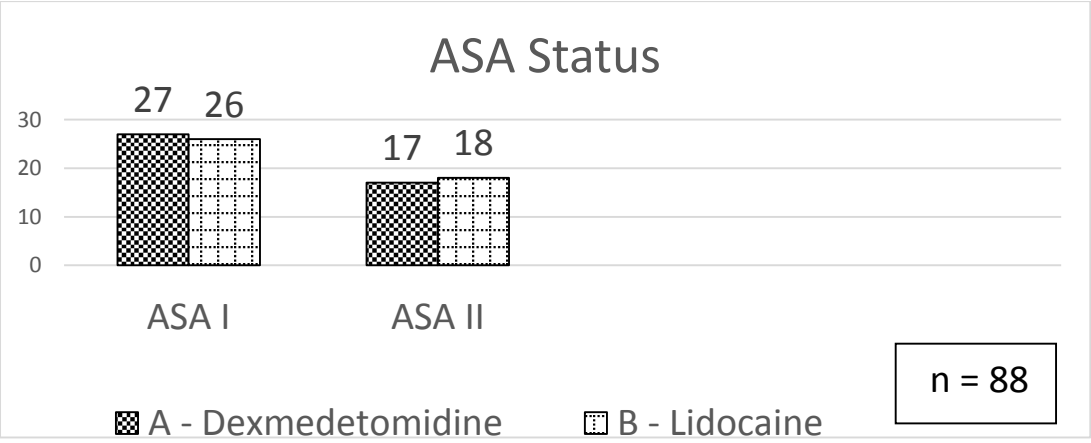
Comorbidities	A - Dexmedetomidine	B – Lidocaine
Diabetes	5	4
Hypertension	3	9
CKD	1	1
Hypothyroidism	8	6
Hyperthyroidism	0	1
Others	1	2



ASA Status:

Out of 88 patients, 53 patients (27 patients in Dexmedetomidine group, 26 patients in Lidocaine group) were ASA category I and 35 patients (17 patients in Dexmedetomidine group, 18 patients in Lidocaine group) were ASA category II. No patient was ASA category III.

ASA Status	A – Dexmedetomidine	B – Lidocaine
ASA I	27	26
ASA II	17	18
ASA III	0	0



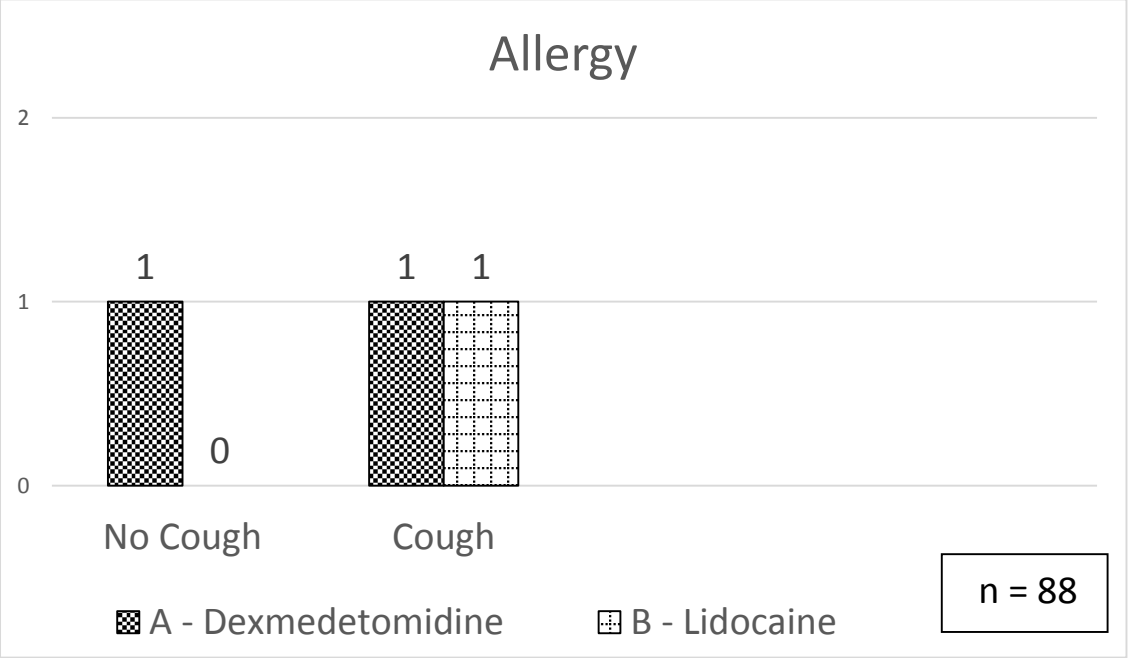
Allergy:

3 out of 88 patients had allergy / atopy, out of which 2 had cough at extubation (1 in each group).

Allergy	A - Dexmedetomidine	B – Lidocaine
Yes	2	1
No	42	43

Allergy n = 3

Cough	A - Dexmedetomidine	B - Lidocaine
Yes	1	1
No	1	0



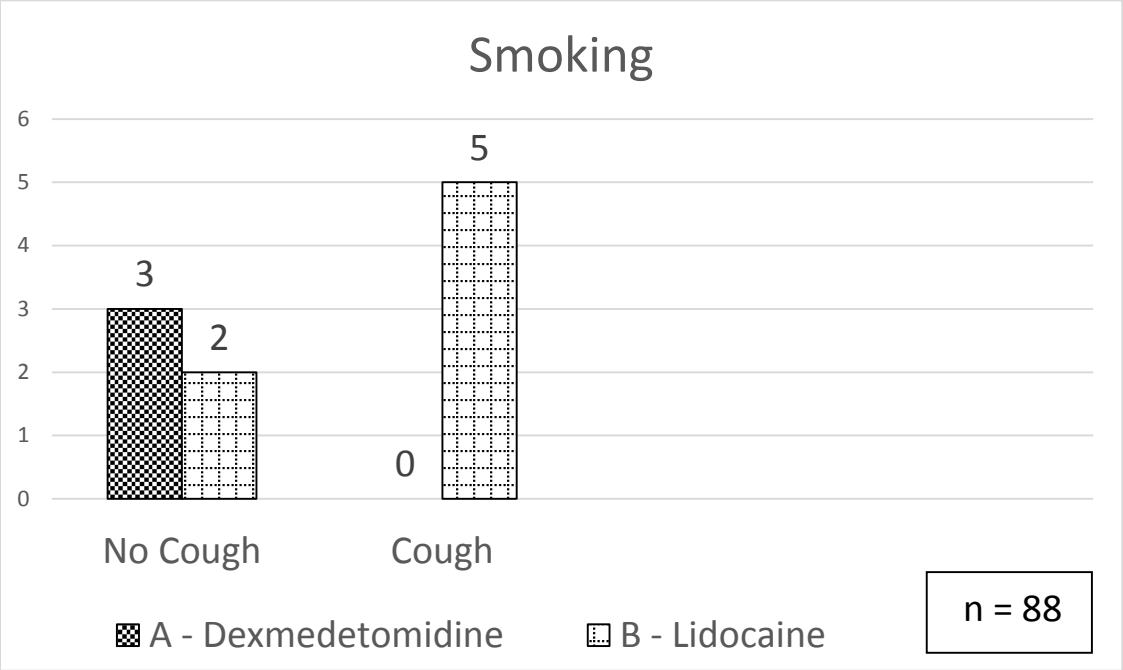
Smoking:

10 out of 88 patients (11.4%) gave histroy of smoking. Out of those 10, 5 had no cough at extubation (3 in Dexmedetomidine group and 2 in Lidocaine group), and 5 had cough at extubation (all 5 in Lidocaine group).

Smoking	A - Dexmedetomidine	B – Lidocaine
Yes	3	7
No	41	37

Smoking n = 10

Cough	A - Dexmedetomidine	B – Lidocaine
Yes	0	5
No	3	2



Tracheal Compression:

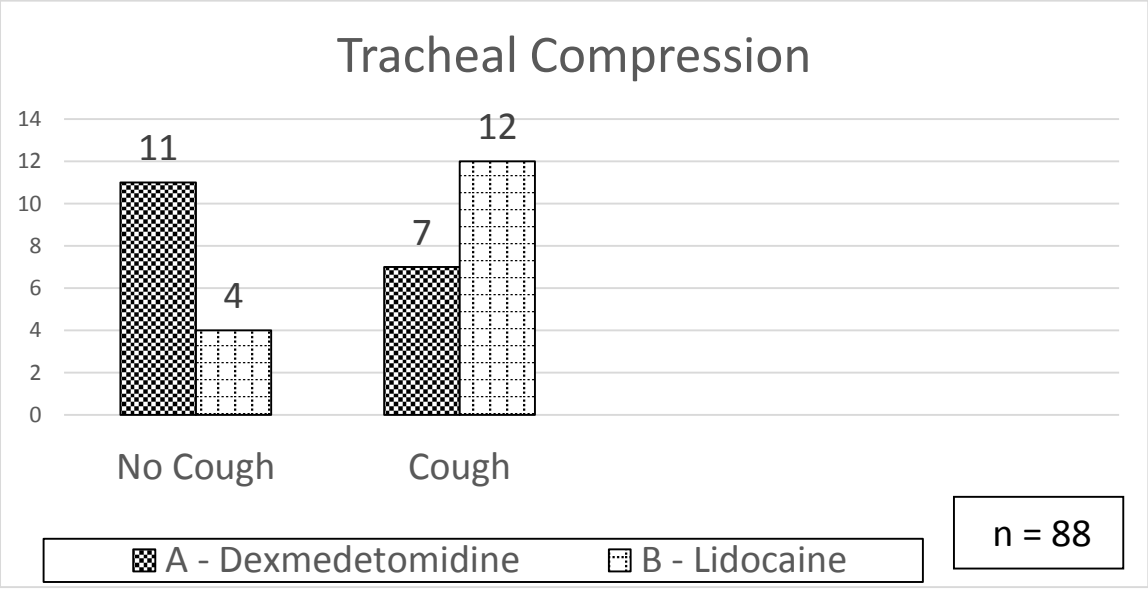
34 patients had compression of the trachea by the thyroid swelling, diagnosed either clinically or by imaging.

Tracheal Compression	A - Dexmedetomidine	B – Lidocaine
Yes	18	16
No	26	28

In the 34 patients with tracheal compression, cough was seen in 19 (55.9%) patients (7 patients in Dexmedetomidine group and 12 in Lidocaine group) and 15 (11 in Dexmedetomidine group and 4 in Lidocaine group) patients (44.1%) had no cough at extubation.

Tracheal Compression n = 34

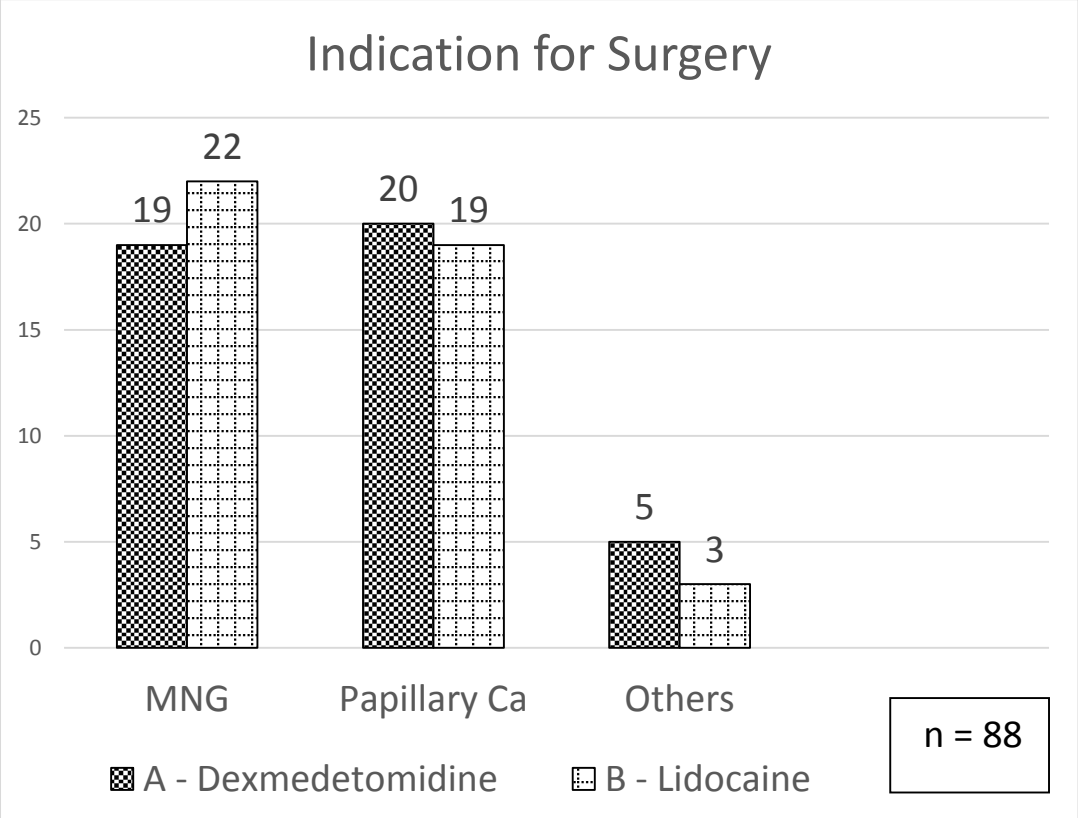
Cough	A - Dexmedetomidine	B – Lidocaine
Yes	7	12
No	11	4



Indication for Surgery:

Majority of patients were operated for multinodular goitre and papillary carcinoma, and the distribution between the study arms were fairly equal.

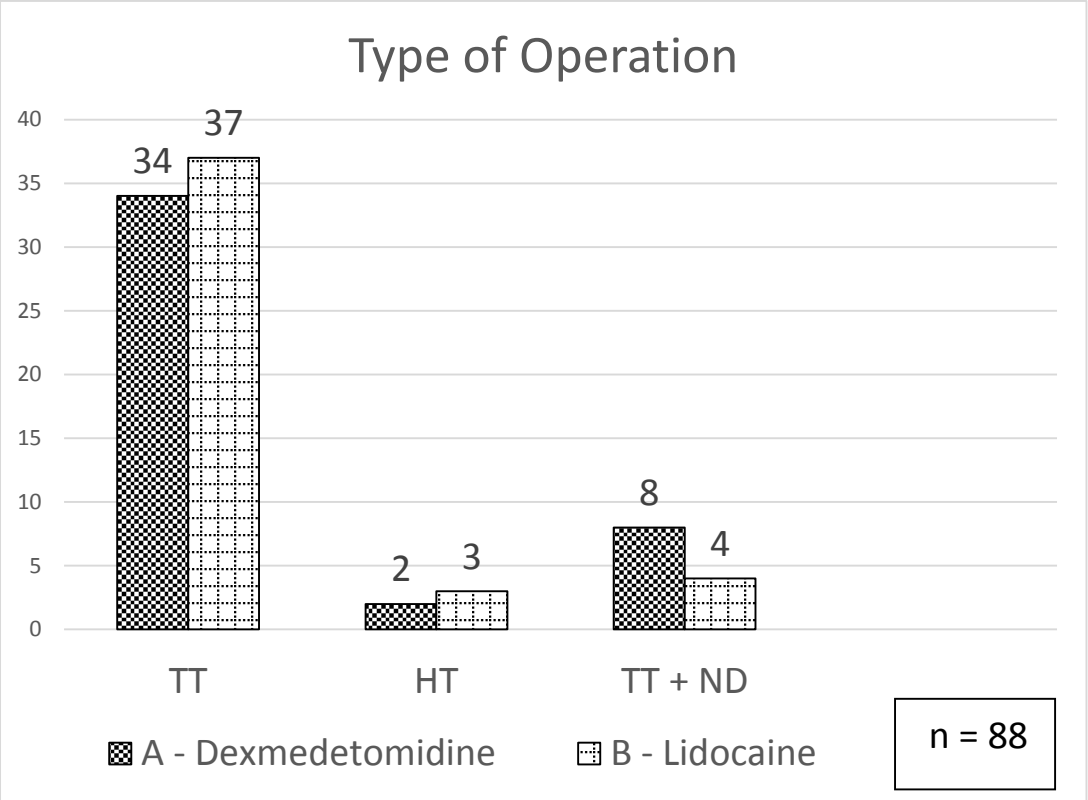
Indication for Surgery	A - Dexmedetomidine	B – Lidocaine
MNG	19	22
Papillary Ca	20	19
Others	5	3



Type of Operation:

71 out of 88 patients had total thyroidectomy (TT) done, 5 patients had hemithyroidectomy (HT), with equal distribution between the two groups. Those patients had both thyroidectomy and neck dissections (12 patients), were more in the Dexmedetomidine group than in Lidocaine group.

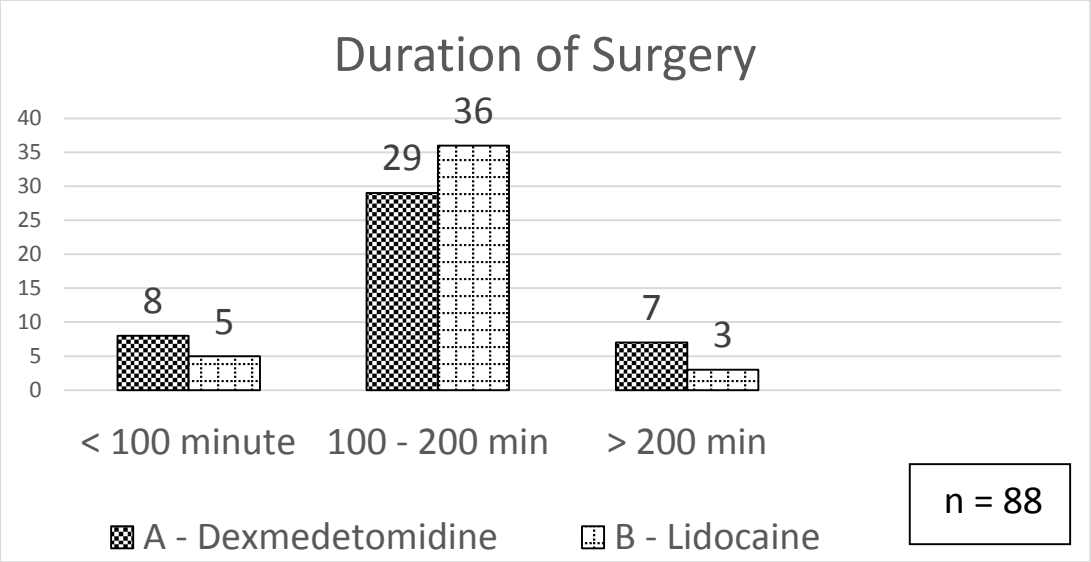
Type of Surgery	A - Dexmedetomidine	B – Lidocaine
TT	34	37
HT	2	3
TT + ND	8	4



Duration of Surgery:

The average duration of surgery was 145.95 minutes. 13 patients had duration of surgery less than 100 minutes (8 in Dexmedetomidine group and 5 in Lidocaine group), 65 patients had duration of surgery between 100 and 200 minutes (29 in Dexmedetomidine group and 36 in Lidocaine group), 10 patients had duration of surgery more than 200 minutes (7 in Dexmedtomidine group and 3 in Lidocaine group).

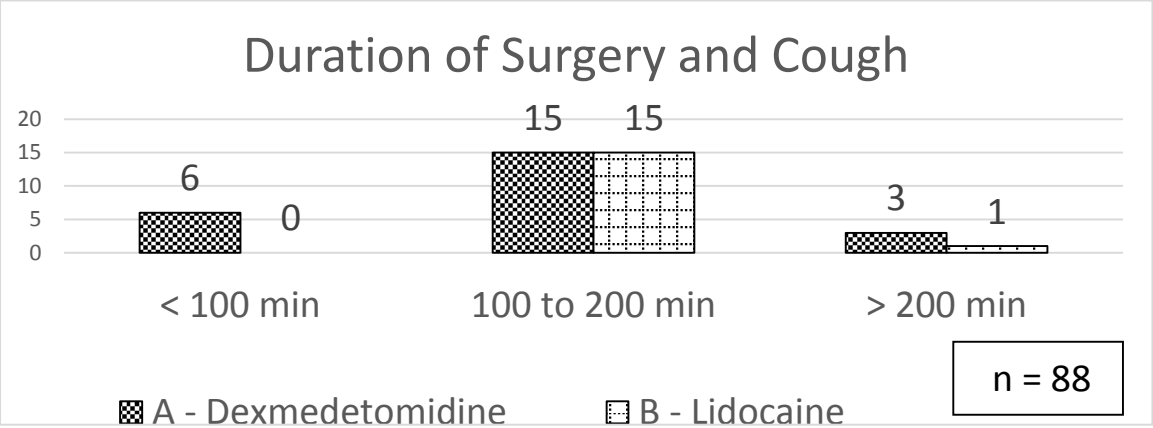
Duration of Surgery	A - Dexmedetomidine	B – Lidocaine
<100 minutes	8	5
100 – 200 minutes	29	36
>200 minutes	7	3



Out of 13 patients with duration of surgery less than 100 minutes, 6 had cough at extubation (all 6 in Dexmedetomidine group) and 7 had no cough at extubation (2 in Dexmedetomidine group and 5 in Lidocaine group). Out of 65 patients with duration of surgery 100 to 200 minutes, 30 had cough (15 in each group), and 35 had

no cough (14 in Dexmedetomidine group and 21 in Lidoacaine group). Out of 10 patients with duration of surgery more than 200 minutes, 4 had cough (3 in Dexmedetomidine group and 1 in Lidocaine group), and 6 had no cough (4 in Dexmedetomidine group and 2 in Lidocaine group).

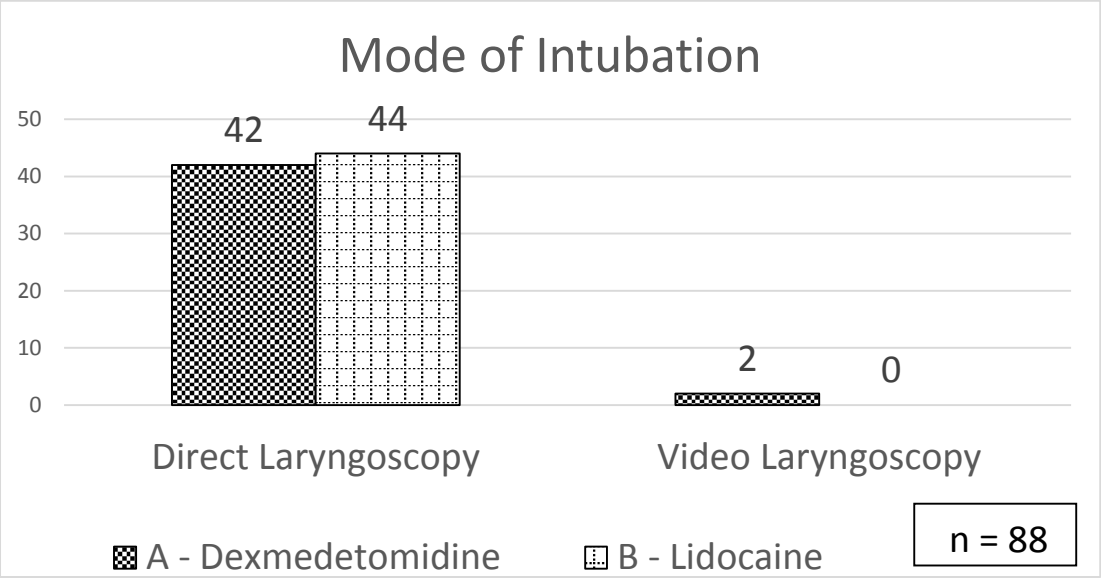
Duration of Surgery	A - Dexmedetomidine		B – Lidocaine	
	Yes Cough	No Cough	Yes Cough	No Cough
<100 minutes	6	2	0	5
100 – 200 minutes	15	14	15	21
>200 minutes	3	4	1	2



Mode of Intubation:

86/88 patients were intubated with direct laryngoscopy using Mcintosh blade. Only 2 patients were intubated with video laryngoscope (Glidescope), (both Dexmedetomidine group).

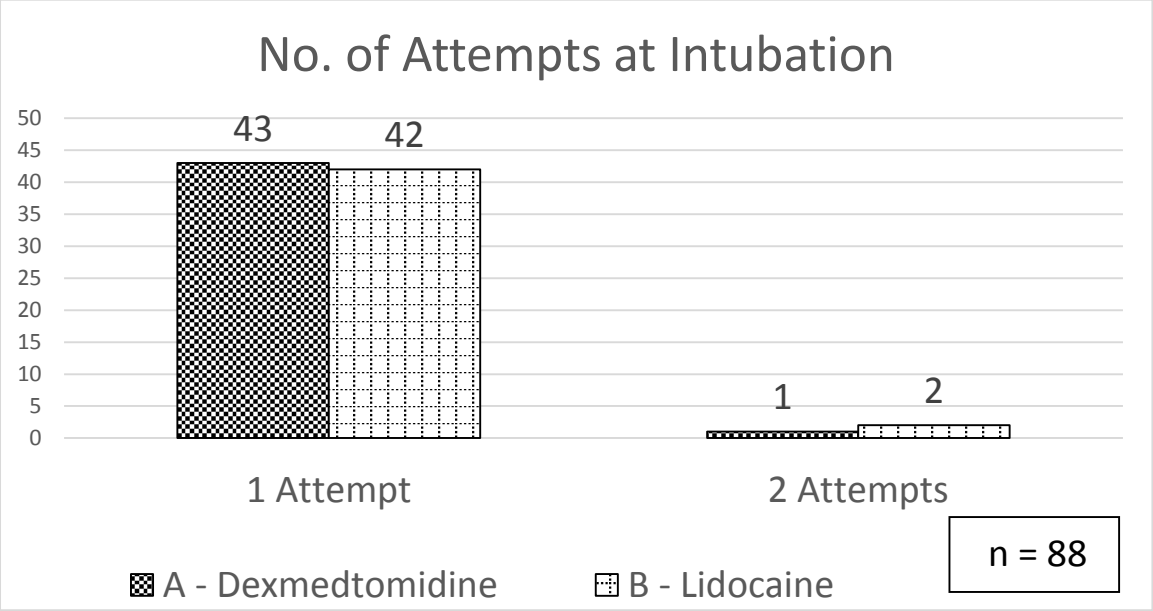
Mode of Intubation	A – Dexmedetomidine	B - Lidocaine
Direct Laryngoscope	42	44
Video Laryngoscope	2	0



Number of Attempts at Intubation:

Out of 88 patients 85 were intubated in one attempt, and 3 patients were intubated in two attempts (1 in Dexmedetomidine group and 2 in Lidocaine group).

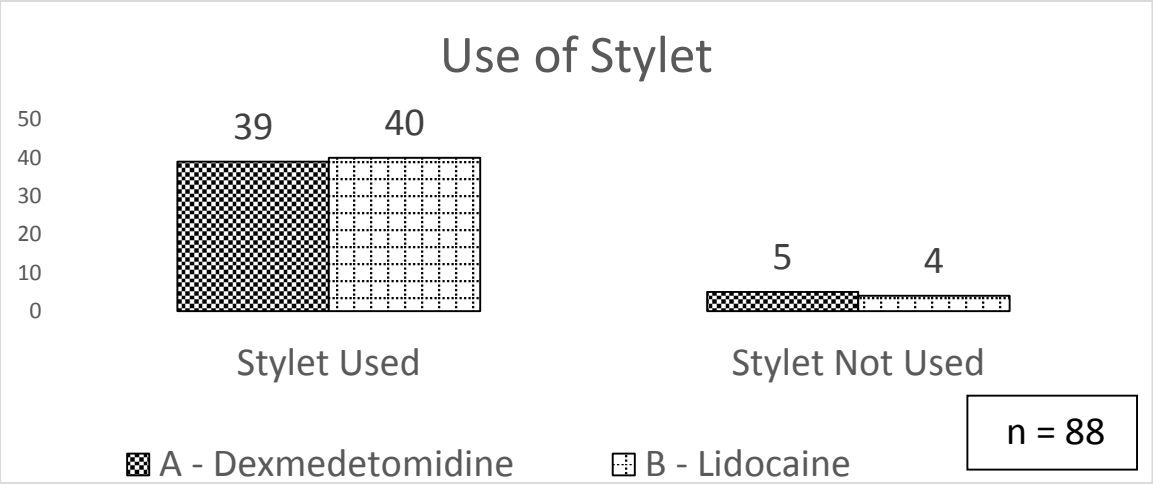
No. of Intubation Attempts	A – Dexmedetomidine	B - Lidocaine
1	43	42
2	1	2



Use of Stylet:

Out of 88 patients, stylet was used in 79 patients (39 patients in Dexmedetomidine group, 40 patients in Lidocaine group). Out of the 79, 44 patients had cough at extubation (21 patients in Dexmedtomidine group and 23 patients in Lidocaine group). Bougie was used for intubation in only one patient out of 88 patients.

Stylet Used	A – Dexmedetomidine	B – Lidocaine
Yes	39	40
No	5	4

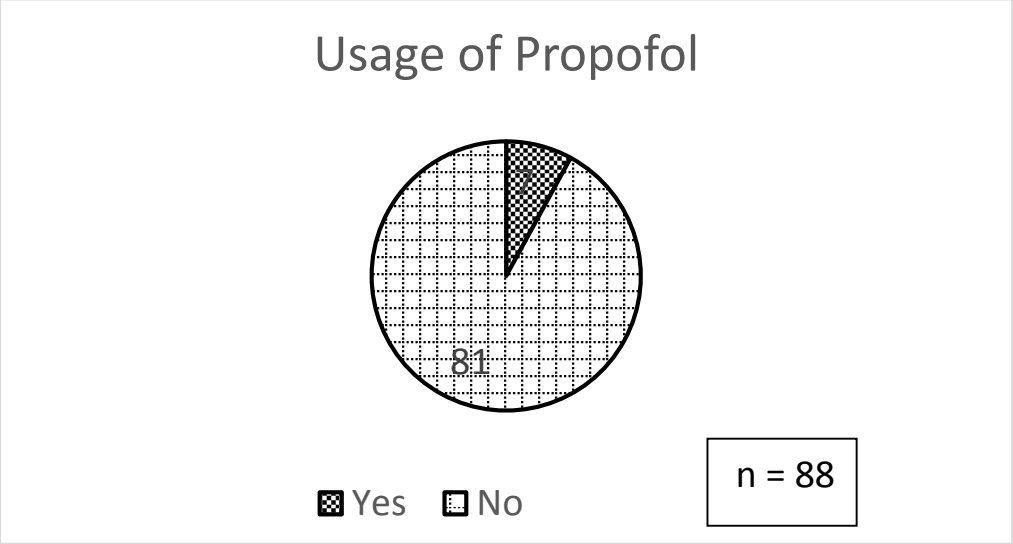


Usage of Propofol towards Extubation:

Propofol was used as a rescue drug to prevent worsening of cough towards extubation in 7 patients (all belonging to Lidocaine group). In 4 patients propofol was used as they moved during closure of skin. 2 patients had grade 2 cough during closure and hence propofol was used. One patient had grade 3 cough 1 minute after extubation for which 30 mg of propofol was given. Out of these 6 patients in whom propofol was used prior to extubation, 4 patients had grade 1 cough at extubation, 2

patients had grade 2 cough at extubation, and 1 patient had grade 3 cough at extubation and at 1 minute from extubation. Out of these 7 patients in whom propofol was used towards extubation, time taken to awaken was 17, 18, 20 minutes in 3 patients, 22 minutes in 2 patients, 26 minutes in 2 patients. No patient in Dexmedetomidine group received propofol towards extubation.

Propofol Used	A – Dexmedetomidine	B - Lidocaine	P value
Yes	0	7	0.006
No	44	37	0.006



Cough in PACU:

Only 1 out of 88 patients had cough in post anaesthesia care unit (PACU). It was one episode of grade 3 cough. This patient belonged to Dexmedtomindine group. This patient had cough at 10 minutes from extubation. There was no external stimulus at that point of time. This patient had no cough at extubation or prior to extubation.

Temperature at Extubation:

All 88 patients had recorded oral temperature of 35.0°C or more. No patient had hypothermia at any point during the surgery and extubation.

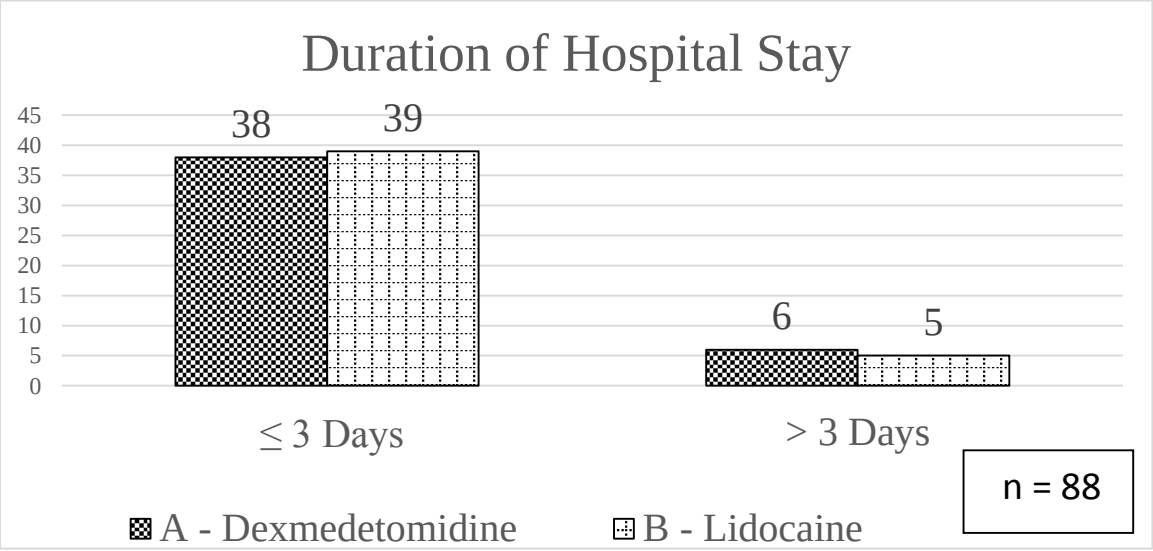
Occurrence of Neck Haematoma / Bleeding:

There was no occurrence of neck haematoma or bleeding in any of the 88 patients in the post-operative period until discharge. However, 1 patient had increased drain output for which the patient was hospitalised for more than 3 days post-operatively.

Duration of Hospital Stay:

11/88 (12.5%) patients (6 in Dexmedtomidine group, 5 in Lidocaine group) were admitted for more than 3 days post-operatively. The reasons were hypocalcaemia (8), chyle leak (1), worsened hoarseness (1) and increased drain output (1).

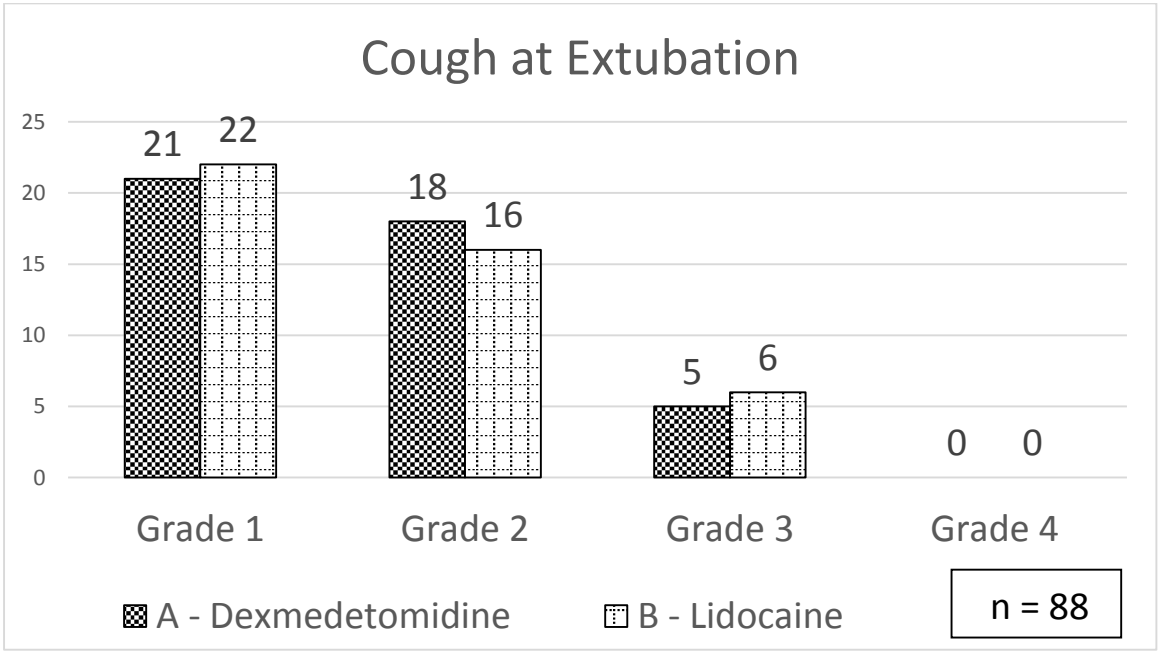
Duration of Hospital Stay	A – Dexmedetomidine	B - Lidocaine	p value
≤ 3 Days	38	39	0.747
>3 Days	6	5	0.747



Cough at Extubation:

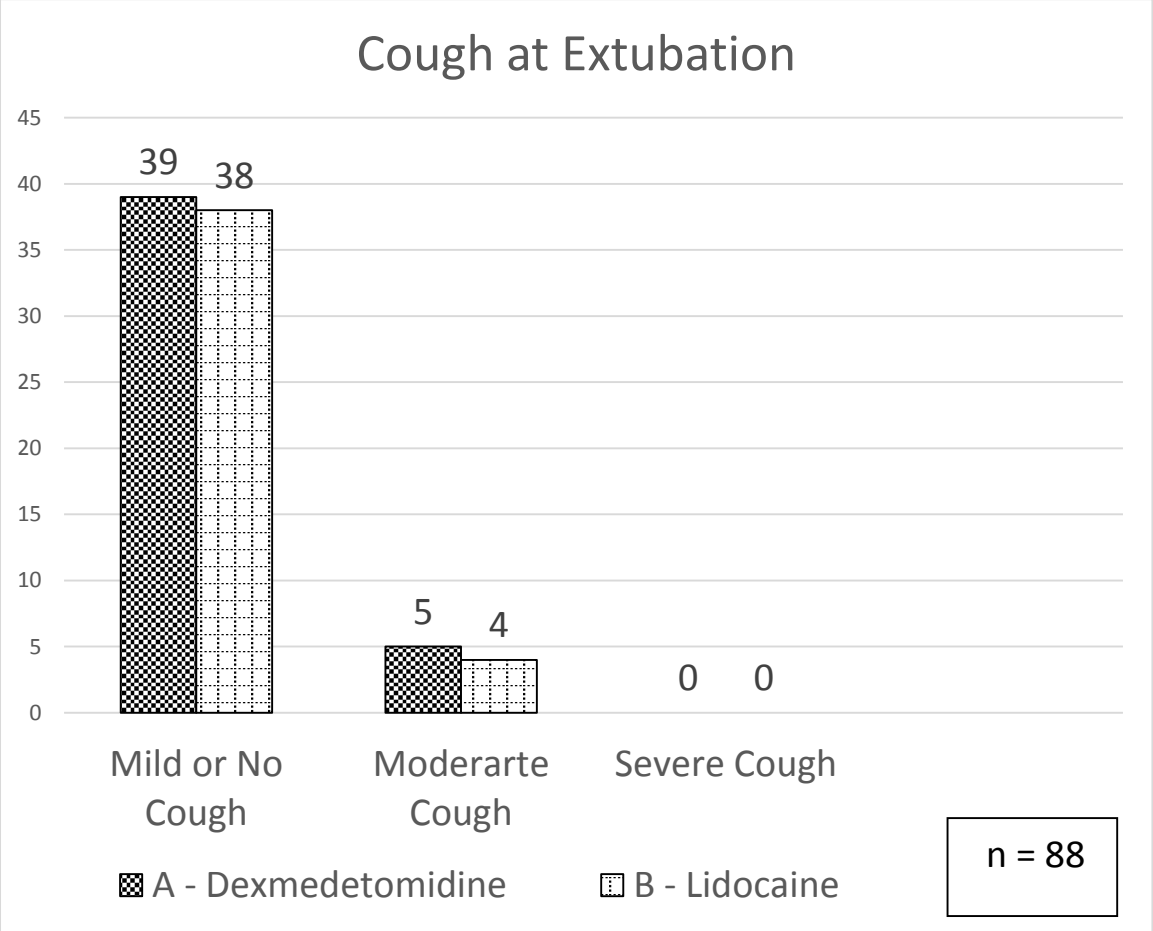
21 out of 44 patients (47.7%) in Dexmedetomidine group had no cough compared to 22 out of 44 patients (50%) in Lidocaine group who had no cough at extubation. 18 out of 44 patients (40.9%) in Dexmedtomidine group had grade 2 cough compared to 16 out of 44 patients (36.4%) in Lidocaine group who had grade 2 cough. 5 patients (11.4%) in Dexmedtomidine group had grade 3 cough, and 6 patients (13.6%) in Lidocaine group had grade 3 cough. No patient had grade 4 cough in either of the groups at extubation.

Cough at Extubation	A - Dexmedetomidine	B – Lidocaine	p value
Grade 1 (No Cough)	21	22	0.831
Grade 2 (Mild Cough)	18	16	0.661
Grade 3 (Moderate Cough)	5	6	0.747
Grade 4 (Severe Cough)	0	0	1.000



39/44 (88.6%) patients in Dexmedtomidine group had mild or no cough compared to 38/44 (86.4) patients in Lidocaine group had mild or no cough. Significant cough (grade 3 cough) occurred in 5/44 (11.4%) patients in Dexmedtomidine group compared to 6/44 (13.6%) patients in Lidocaine group.

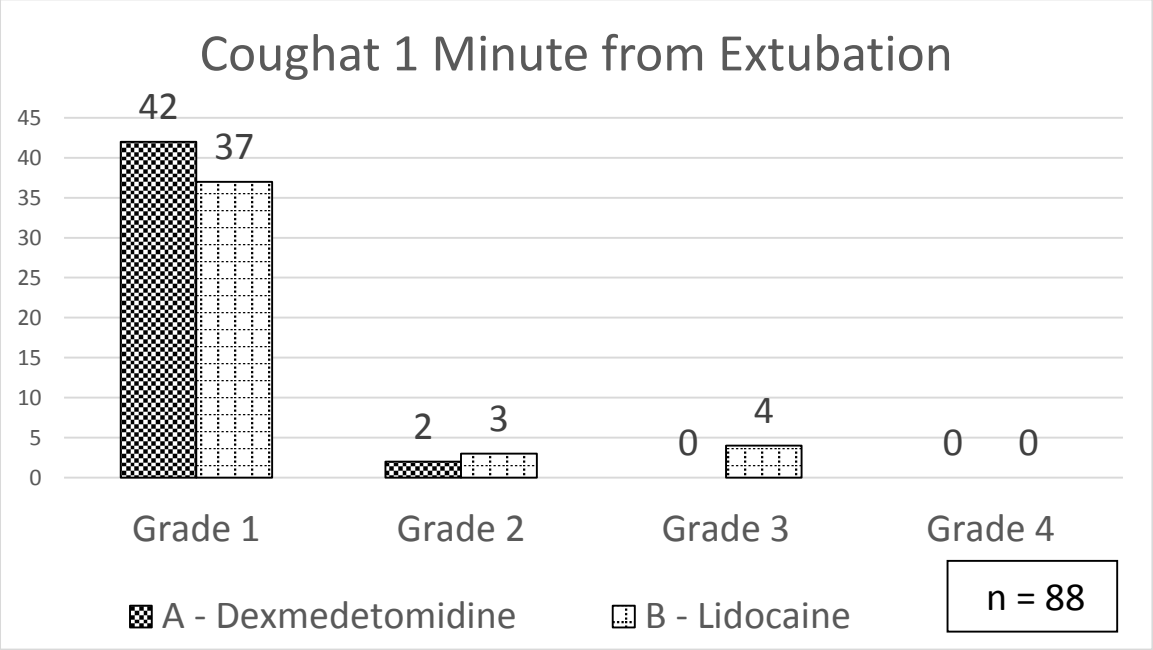
Cough at Extubation	A - Dexmedetomidine	B – Lidocaine	p value
Mild or No Cough	39	38	0.747
Moderate Cough	5	6	0.747
Severe Cough	0	0	1.000



Cough at 1 Minute from Extubation:

42 out of 44 patients (95.5%) in Dexmedtomidine group had no cough compared to 37 out of 44 patients (84.1%) in Lidocaine group who had no cough at 1 minute from extubation. 2 out of 44 patients (4.5%) had grade 2 cough in Dexmedtomidine group compared to 3 out of 44 patients (6.8%) in Lidocaine group who had grade 2 cough. No patient in Dexmedtomidine group had grade 3 cough, and 4 patients (9.1%) in Lidocaine group had grade 3 cough. No patient had grade 4 cough in either of the groups at 1 minute from extubation.

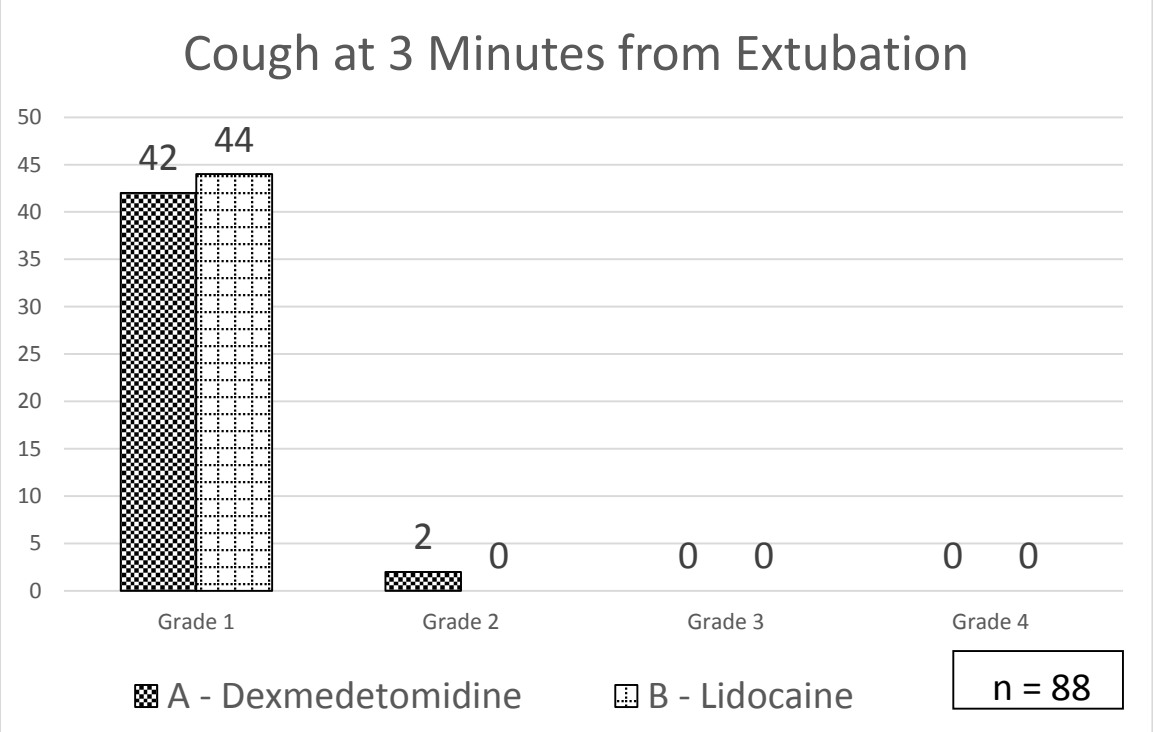
Cough at 1 minute	A - Dexmedetomidine	B – Lidocaine	p value
Grade 1 (No Cough)	42	37	0.079
Grade 2 (Mild Cough)	2	3	0.645
Grade 3 (Moderate Cough)	0	4	0.041
Grade 4 (Severe Cough)	0	0	1.000



Cough at 3 Minutes from Extubation:

42 out of 44 patients (95.5%) in Dexmedtomidine group had no cough compared to all 44 patients (100%) in Lidocaine group who had no cough at 3 minute from extubation. 2 out of 44 patients (4.5%) had grade 2 cough in Dexmedtomidine group compared to no patient in Lidocaine group who had grade 2 cough. No patient had grade 3 or grade 4 cough in either of the groups at 3 minute from extubation.

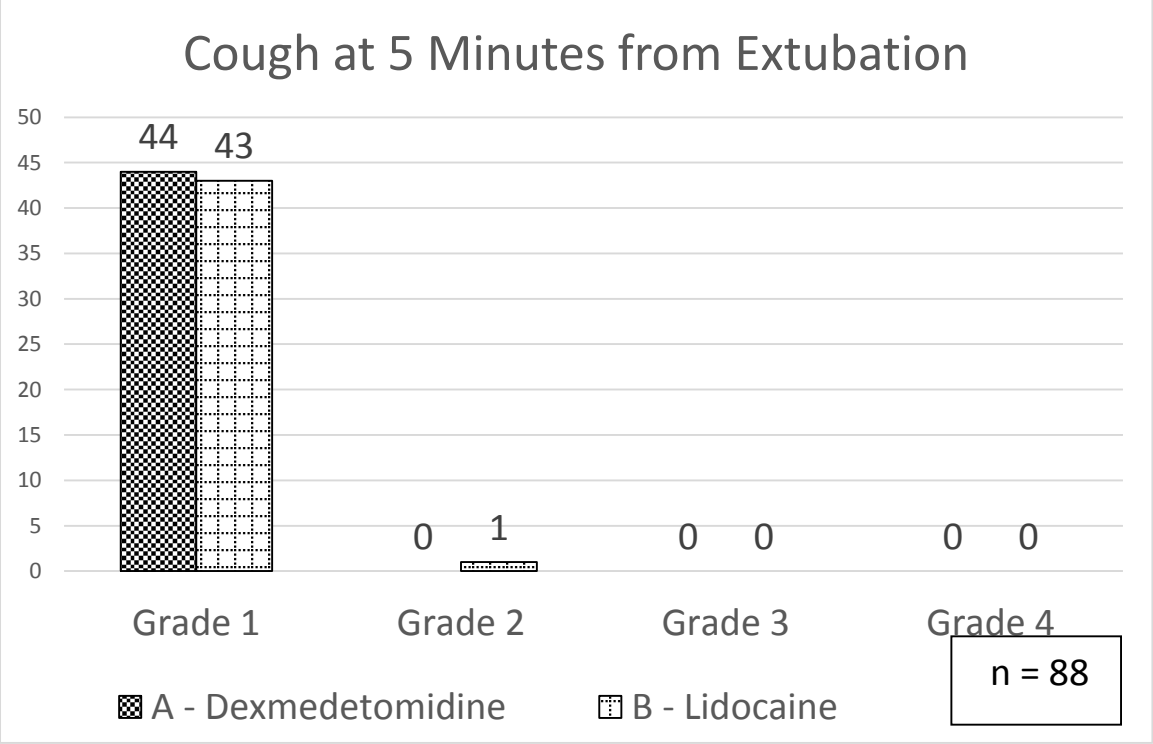
Cough at 3 minutes	A - Dexmedetomidine	B – Lidocaine	p value
Grade 1 (No Cough)	42	44	0.153
Grade 2 (Mild Cough)	2	0	0.153
Grade 3 (Moderate Cough)	0	0	1.000
Grade 4 (Severe Cough)	0	0	1.000



Cough at 5 Minutes from Extubation:

All 44 patients (100%) in Dexmedtomidine group had no cough compared to 43 out of 44 patients (97.7%) in Lidocaine group who had no cough at 5 minutes from extubation. No patient had grade 2 cough in Dexmedtomidine group compared to 1 out of 44 patients (2.3%) in Lidocaine group who had grade 2 cough. No patient had grade 3 or grade 4 cough in either of the groups at 5 minutes from extubation.

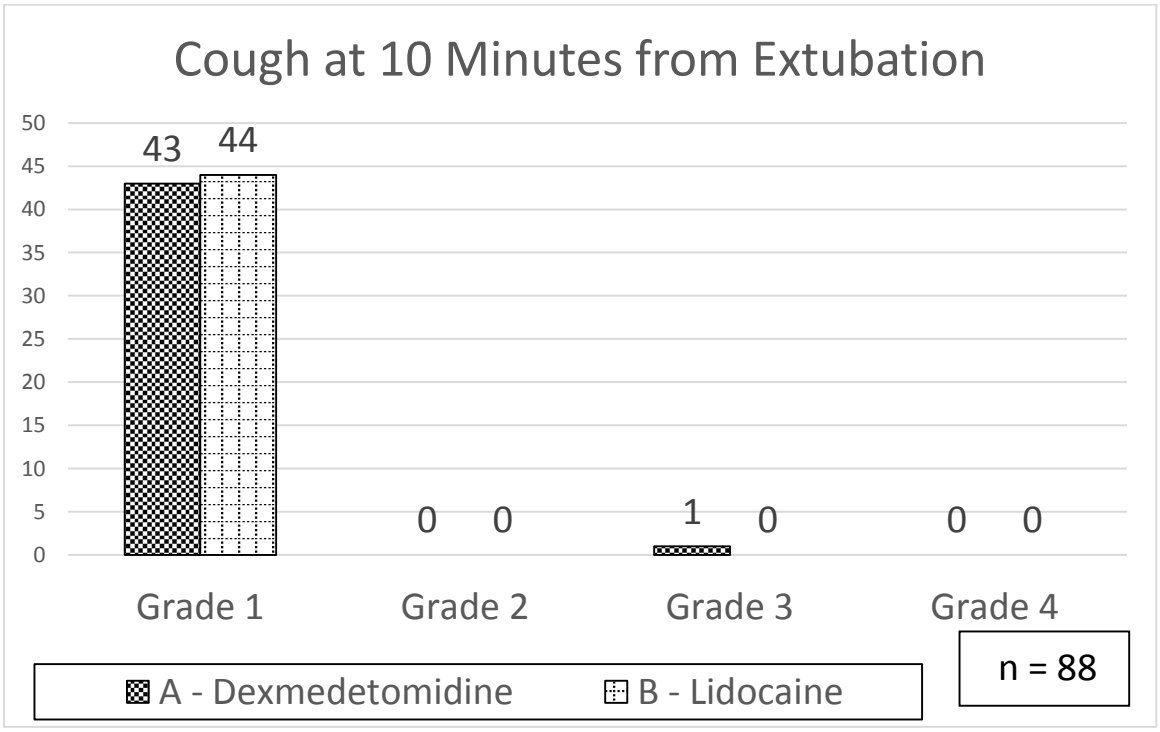
Cough at 5 minutes	A - Dexmedetomidine	B – Lidocaine	p value
Grade 1 (No Cough)	44	43	0.314
Grade 2 (Mild Cough)	0	1	0.314
Grade 3 (Moderate Cough)	0	0	1.000
Grade 4 (Severe Cough)	0	0	1.000



Cough at 10 Minutes from Extubation:

43 out of 44 patients (97.7%) in Dexmedtomidine group had no cough compared to all 44 patients (100%) in Lidocaine group who had no cough at 10 minutes from extubation. No patient had grade 2 cough in either of the groups. 1 patient (2.3%) had grade 3 cough in Dexmedtomidine group, and no patient had grade 3 cough in Lidocaine group. No patient had grade 4 cough in either of the groups at 10 minutes from extubation.

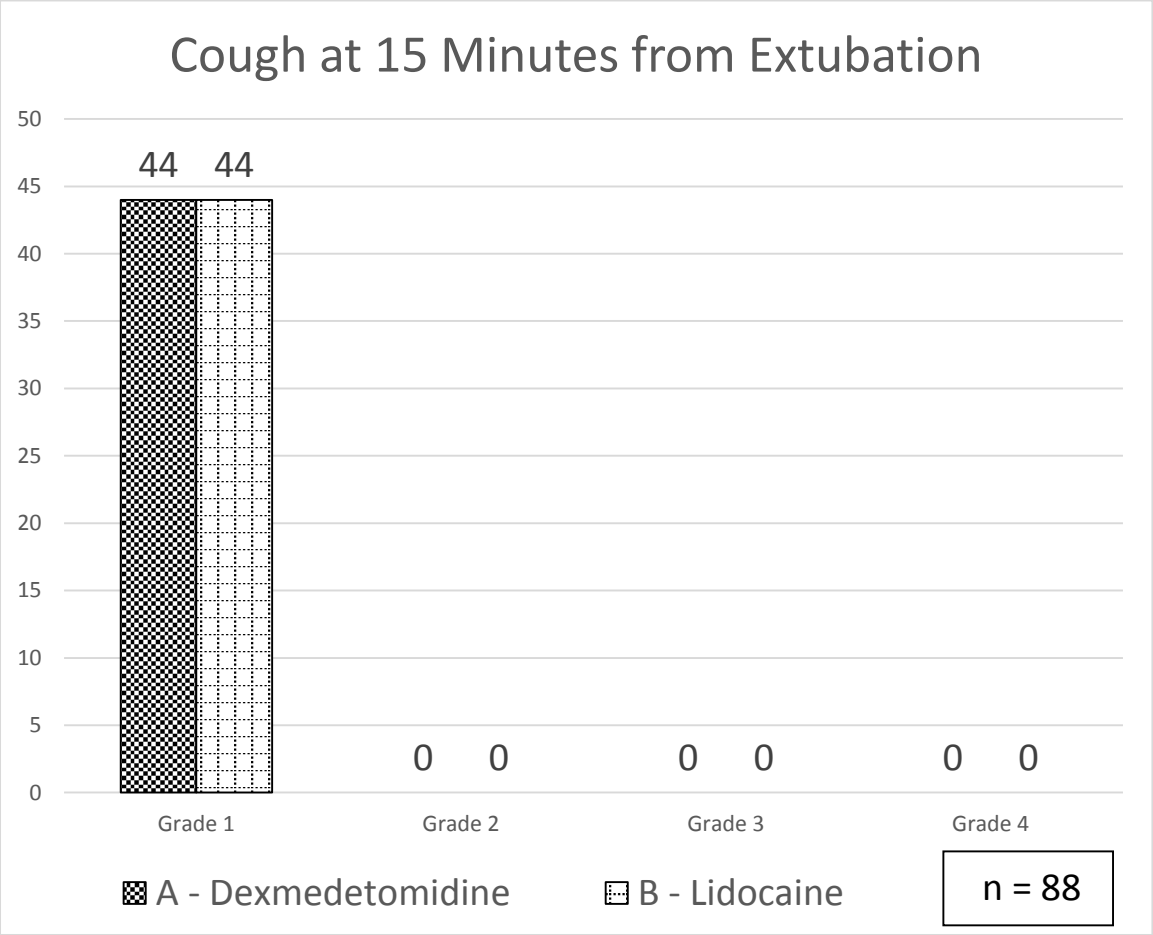
Cough at 10 minutes	A - Dexmedetomidine	B – Lidocaine	p value
Grade 1 (No Cough)	43	44	0.314
Grade 2 (Mild Cough)	0	0	1.000
Grade 3 (Moderate Cough)	1	0	0.314
Grade 4 (Severe Cough)	0	0	1.000



Cough at 15 Minutes from Extubation:

No patient had any cough in either of the groups at 15 minutes from extubation.

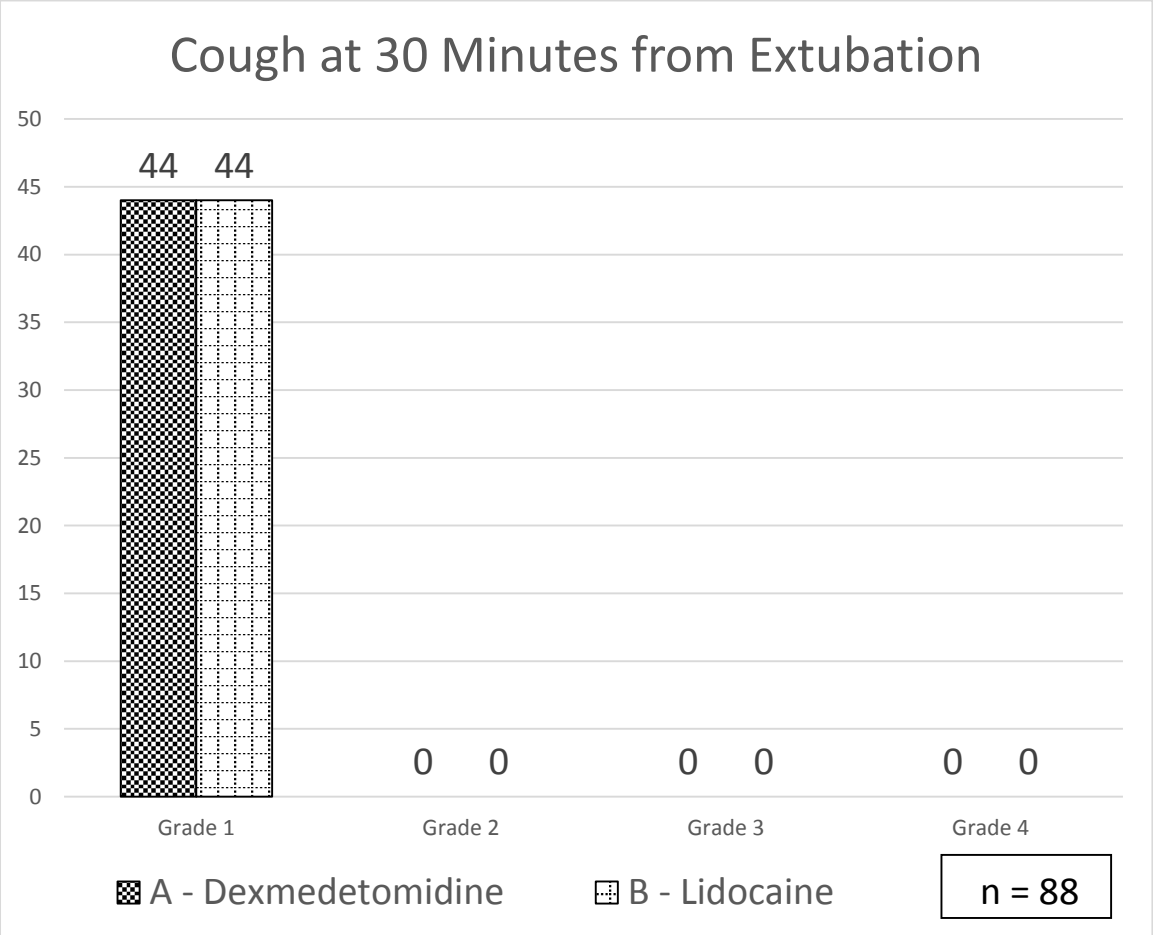
Cough at 15 minutes	A - Dexmedetomidine	B – Lidocaine	p value
Grade 1 (No Cough)	44	44	1.000
Grade 2 (Mild Cough)	0	0	1.000
Grade 3 (Moderate Cough)	0	0	1.000
Grade 4 (Severe Cough)	0	0	1.000



Cough at 30 Minutes from Extubation:

No patient had any cough in either of the groups at 30 minutes from extubation.

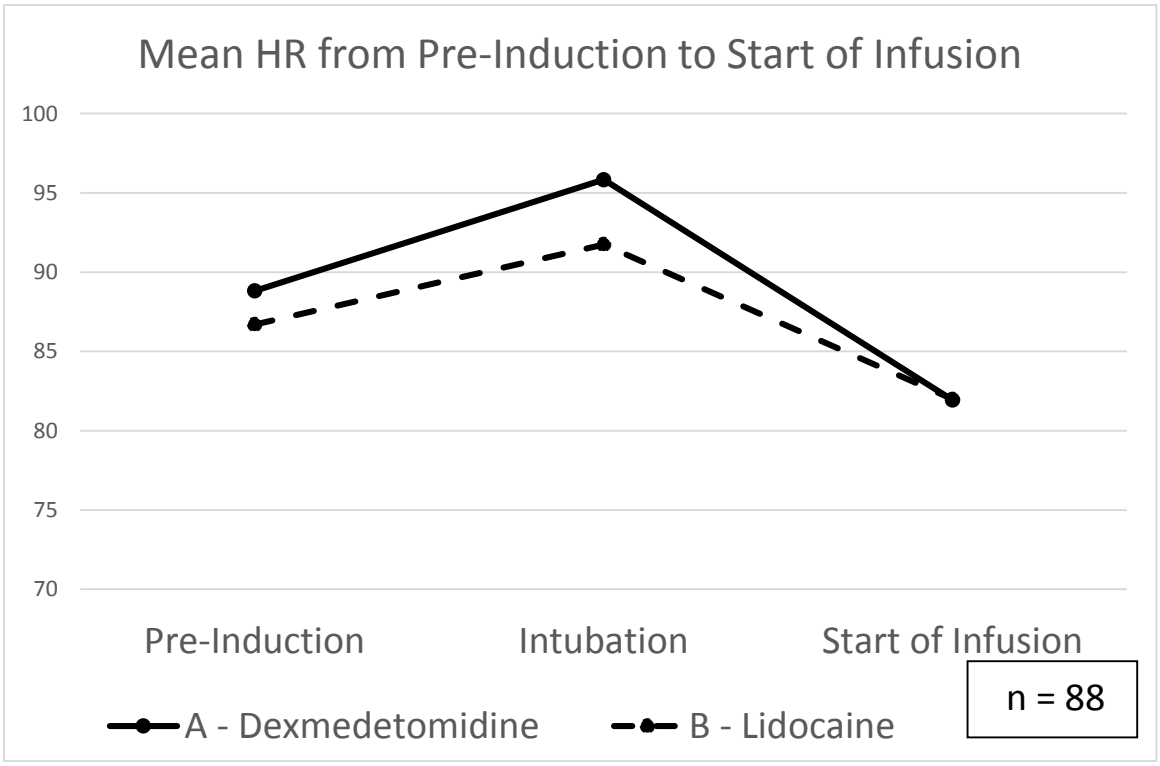
Cough at 30 minutes	A - Dexmedetomidine	B – Lidocaine	p value
Grade 1 (No Cough)	44	44	1.000
Grade 2 (Mild Cough)	0	0	1.000
Grade 3 (Moderate Cough)	0	0	1.000
Grade 4 (Severe Cough)	0	0	1.000



Mean Heart Rate from Pre-Induction to Start of Infusion:

The mean heart rate per minute (HR) at pre-induction in Dexmedtomidine group was 88.82, and in Lidocaine group was 86.70. At intubation it was 95.84 in Dexmedtomidine group and 91.75 in Lidocaine group. At the time of start of the infusion the mean heart rate in Dexmedtomidine group was 81.93, and in Lidocaine group was 81.98.

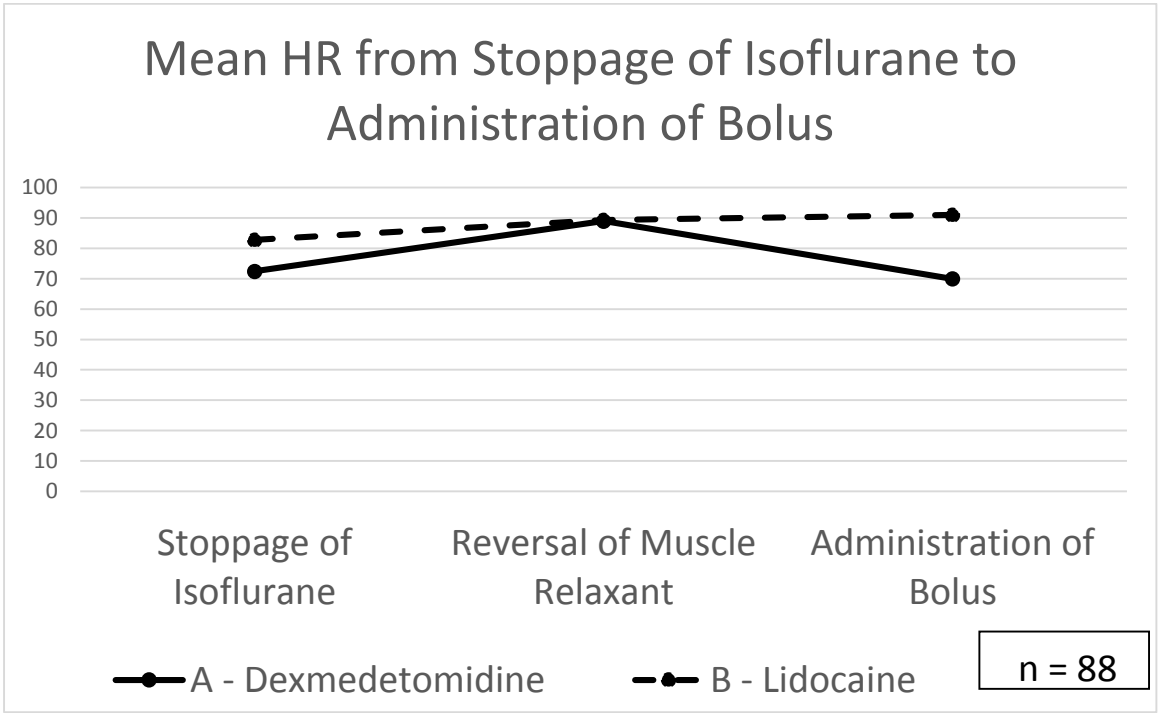
Mean Heart Rate	A - Dexmedetomidine	B – Lidocaine	p value
Pre-Induction	88.82	86.70	0.430
Intubation	95.84	91.75	0.165
Start of Infusion	81.93	81.98	0.985



Mean Heart Rate from Stoppage of Isoflurane to Administration of Bolus:

The mean heart rate per minute (HR) at stoppage of isoflurane in Dexmedetomidine group was 72.41, and in Lidocaine group was 82.75. At administration of reversal of muscle relaxant, it was 88.95 in Dexmedetomidine group and 89.30 in Lidocaine group. At the time of administration of bolus, the mean heart rate in Dexmedtomidine group was 69.93, and in Lidocaine group was 90.98.

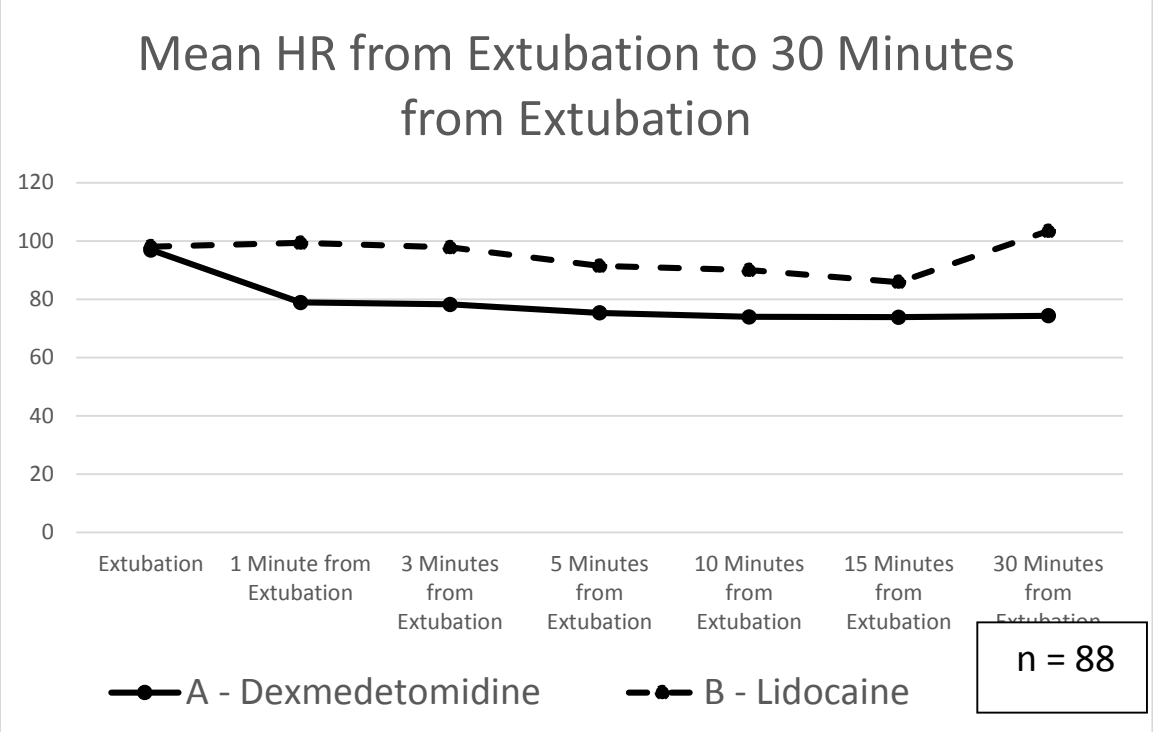
Mean Heart Rate	A - Dexmedetomidine	B – Lidocaine	p value
Stoppage of Isoflurane	72.41	82.75	0.001
Reversal of Muscle Relaxant	88.95	89.30	0.984
Bolus Admisitration	69.93	90.98	0.000



Mean Heart Rate from Extubation to 30 minutes from Extubation:

The mean heart rate per minute (HR) at extubation in Dexmedetomidine group was 96.91, and in Lidocaine group was 98.07. At 1 minute from extubation it was 78.91 in Dexmedetomidine group and 99.32 in Lidocaine group. At 3 minutes from extubation it was 78.23 in Dexmedetomidine group and 97.82 in Lidocaine group. At 5 minutes from extubation it was 75.36 in Dexmedetomidine group and 91.43 in Lidocaine group. At 10 minutes from extubation it was 73.98 in Dexmedetomidine group A and 90.00 in Lidocaine group. At 15 minutes from extubation it was 73.86 in Dexmedetomidine group and 85.89 in Lidocaine group. At 30 minute from extubation it was 74.36 in Dexmedetomidine group and 103.39 in Lidocaine group.

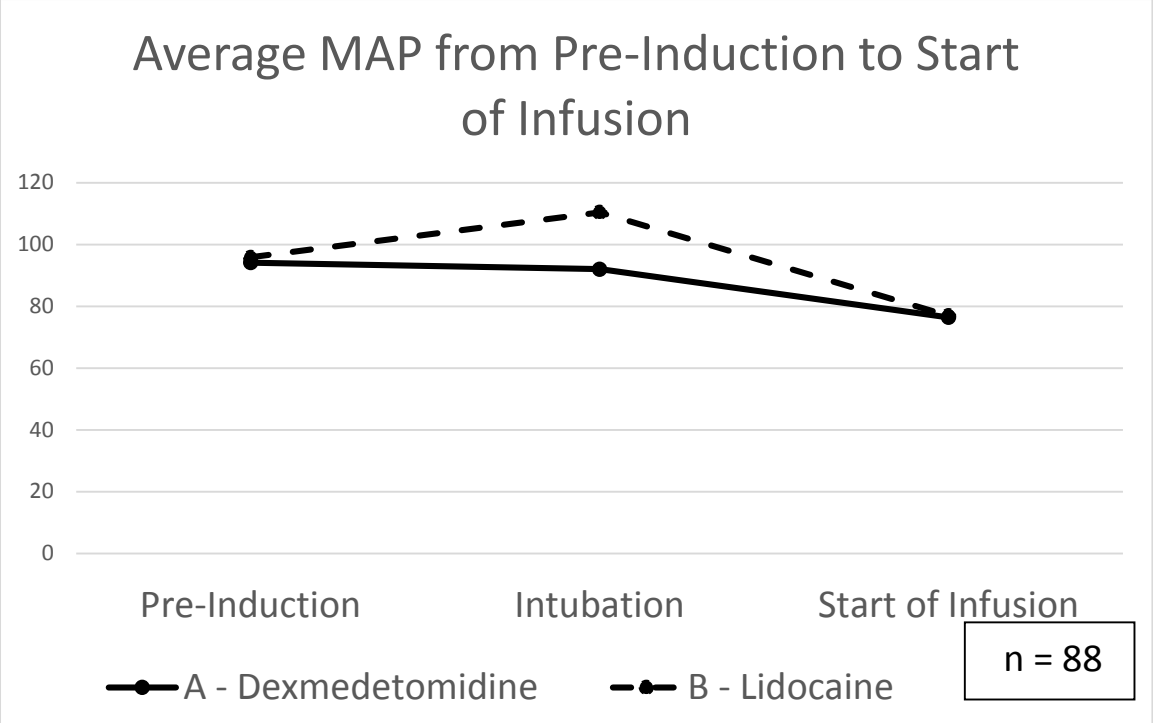
Mean Heart Rate	A - Dexmedetomidine	B – Lidocaine	p value
Extubation	96.91	98.07	0.953
1 Minute from Extubation	78.91	99.32	0.000
3 Minute from Extubation	78.23	97.82	0.000
5 Minute from Extubation	75.36	91.43	0.000
10 Minute from Extubation	73.98	90.00	0.000
15 Minute from Extubation	73.86	85.89	0.000
30 Minute from Extubation	74.36	103.39	0.097



Average Mean Arterial Pressure from Pre-Induction to Start of Infusion:

The average mean arterial pressure in mm Hg (MAP) at pre-induction in Dexmedetomidine group was 94.14, and in Lidocaine group was 95.86. At intubation it was 92.00 in Dexmedetomidine group and 110.41 in Lidocaine group. At the time of start of the infusion the average MAP in Dexmedetomidine group was 76.41, and in Lidocaine group was 76.93.

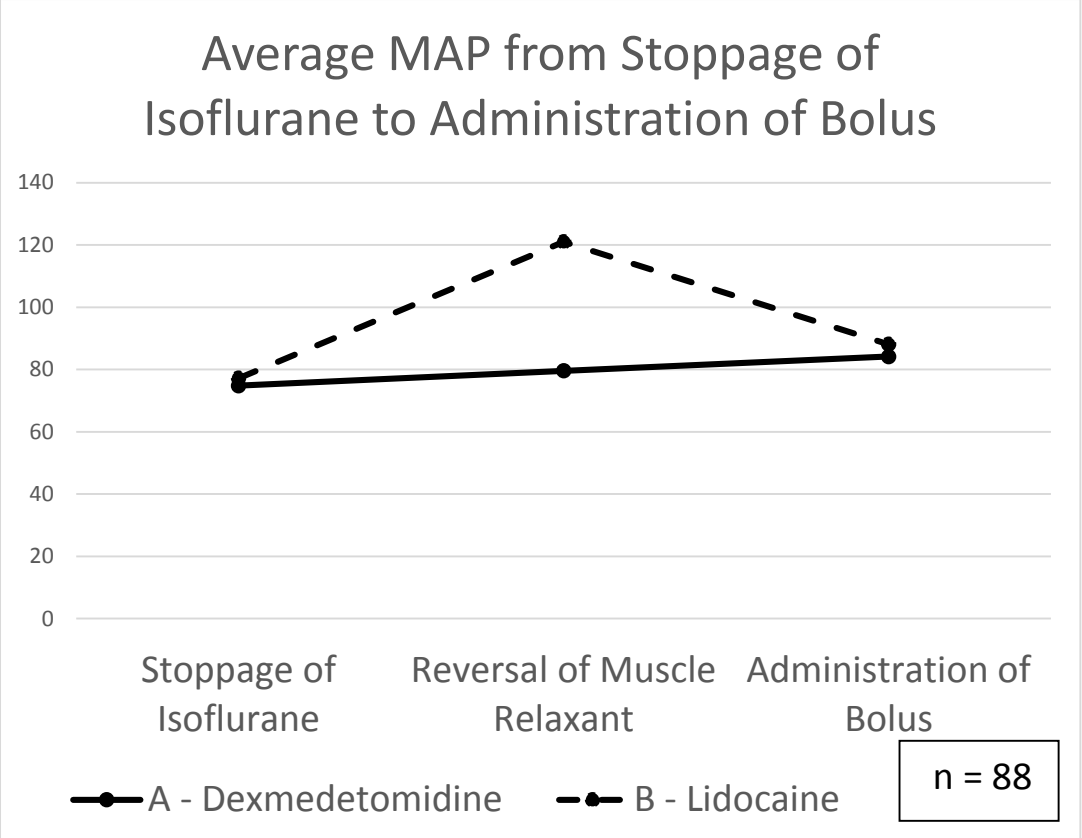
Average MAP	A - Dexmedetomidine	B – Lidocaine	p value
Pre-Induction	94.14	95.86	0.505
Intubation	92.00	110.41	0.254
Start of Infusion	76.41	76.93	0.827



Average MAP from Stoppage of Isoflurane to Administration of Bolus:

The average MAP in mm Hg at stoppage of isoflurane in Dexmedetomidine group was 74.80, and in Lidocaine group was 77.20. At administration of reversal of muscle relaxant, it was 79.57 in Dexmedetomidine group and 121.00 in Lidocaine group. At the time of administration of bolus, the average MAP in Dexmedetomidine group was 84.18, and in Lidocaine group was 88.11.

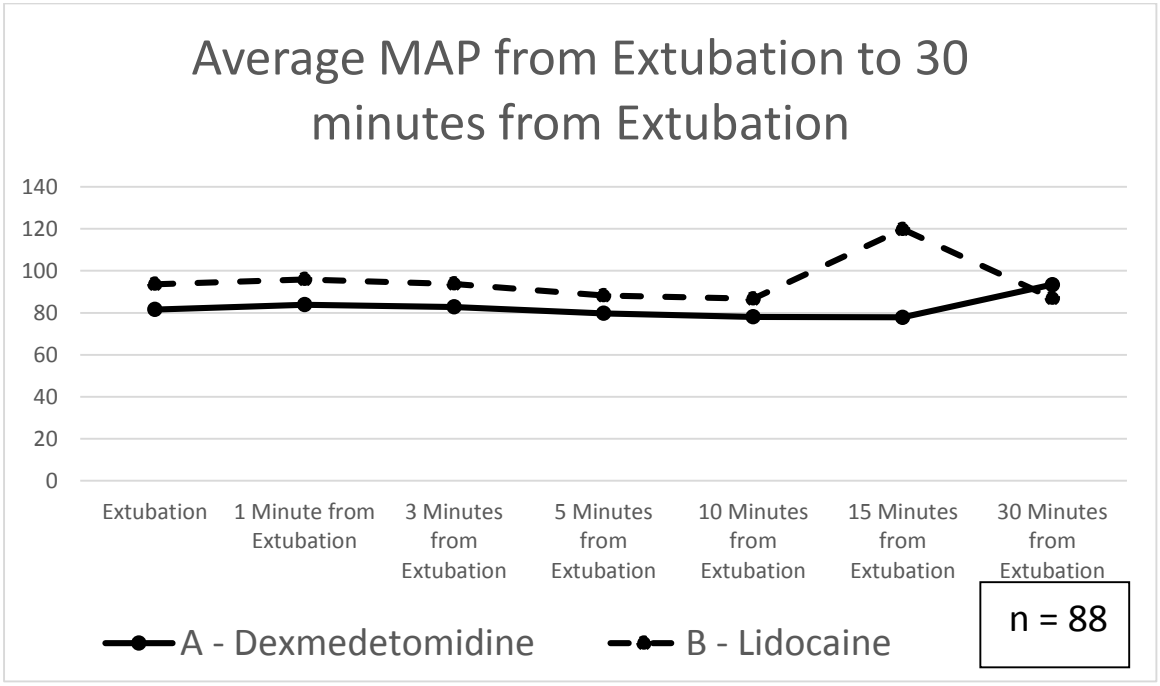
Average MAP	A - Dexmedetomidine	B – Lidocaine	p value
Stoppage of Isoflurane	74.80	77.20	0.284
Reversal of Muscle Relaxant	79.57	121.00	0.089
Bolus Admisitration	84.18	88.11	0.121



Average MAP from Extubation to 30 minutes from Extubation:

The average MAP in mm Hg at extubation in Dexmedetomidine group was 81.59, and in Lidocaine group was 93.61. At 1 minute from extubation it was 83.86 in Dexmedetomidine group and 95.89 in Lidocaine group. At 3 minutes from extubation it was 82.77 in Dexmedetomidine group and 93.77 in Lidocaine group. At 5 minutes from extubation it was 79.77 in Dexmedetomidine group and 88.23 in Lidocaine group. At 10 minutes from extubation it was 78.09 in Dexmedetomidine group and 86.66 in Lidocaine group. At 15 minutes from extubation it was 77.84 in Dexmedetomidine group and 119.82 in Lidocaine group. At 30 minute from extubation it was 93.39 in Dexmedetomidine group and 87.00 in Lidocaine group.

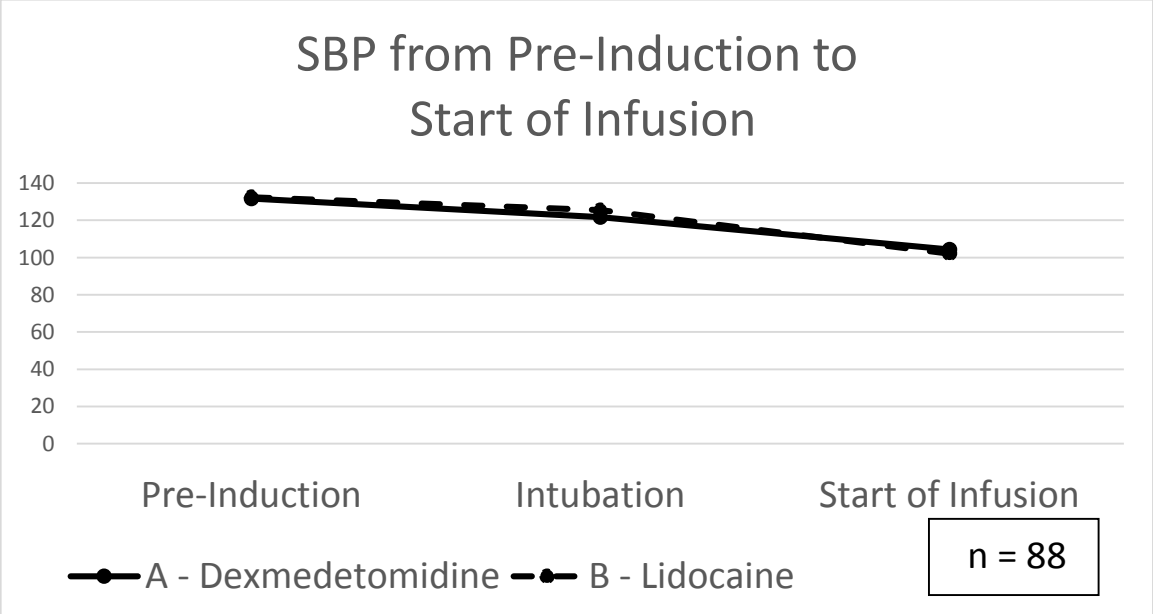
Average MAP	A - Dexmedetomidine	B – Lidocaine	p value
Extubation	81.59	93.61	0.000
1 Minute from Extubation	83.86	95.89	0.000
3 Minute from Extubation	82.77	93.77	0.000
5 Minute from Extubation	79.77	88.23	0.001
10 Minute from Extubation	78.09	86.66	0.001
15 Minute from Extubation	77.84	119.82	0.079
30 Minute from Extubation	93.39	87.00	0.656



Mean Systolic Pressure from Pre-Induction to Start of Infusion:

The mean systolic blood pressure in mm Hg (SBP) at pre-induction in Dexmedetomidine group was 131.68, and in Lidocaine group was 132.41. At intubation it was 121.70 in Dexmedetomidine group and 125.45 in Lidocaine group. At the time of start of the infusion the mean SBP in Dexmedetomidine group was 104.34, and in Lidocaine group was 102.16.

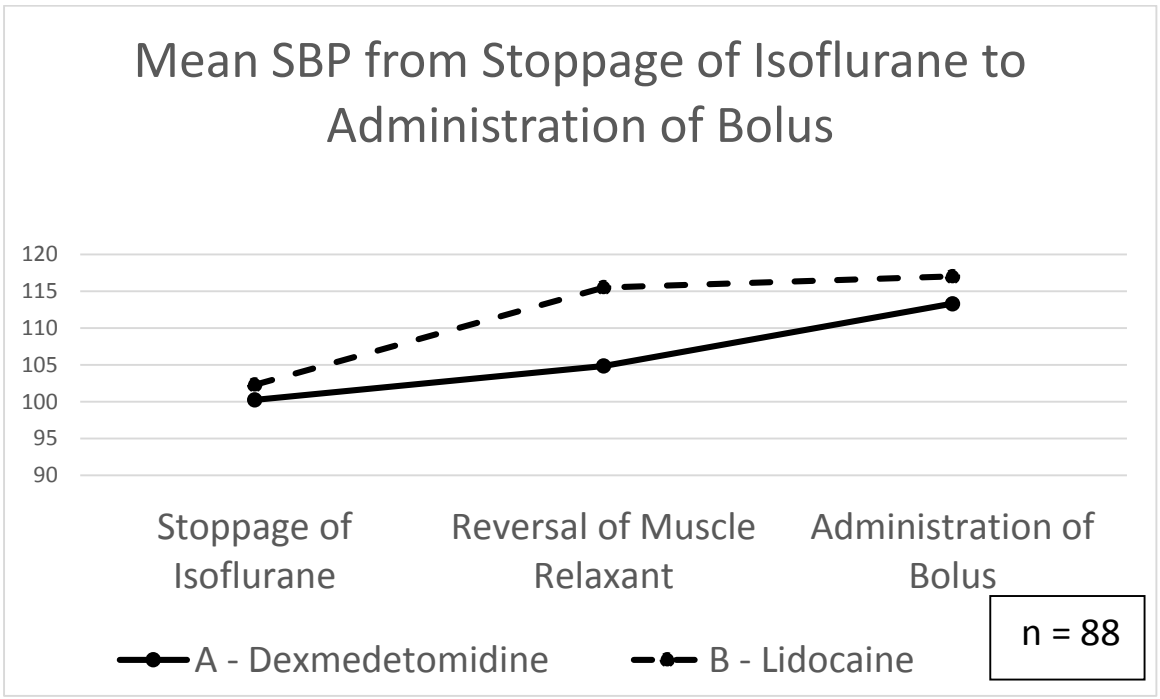
Mean SBP	A - Dexmedetomidine	B – Lidocaine	p value
Pre-Induction	131.68	132.41	0.857
Intubation	121.70	125.45	0.453
Start of Infusion	104.34	102.16	0.434



Mean SBP from Stoppage of Isoflurane to Administration of Bolus:

The mean SBP in mm Hg at stoppage of isoflurane in Dexmedetomidine group was 100.25, and in Lidocaine group was 102.30. At administration of reversal of muscle relaxant, it was 104.86 in Dexmedetomidine group and 115.52 in Lidocaine group. At the time of administration of bolus, the mean SBP in Dexmedetomidine group was 113.32, and in Lidocaine group was 117.02.

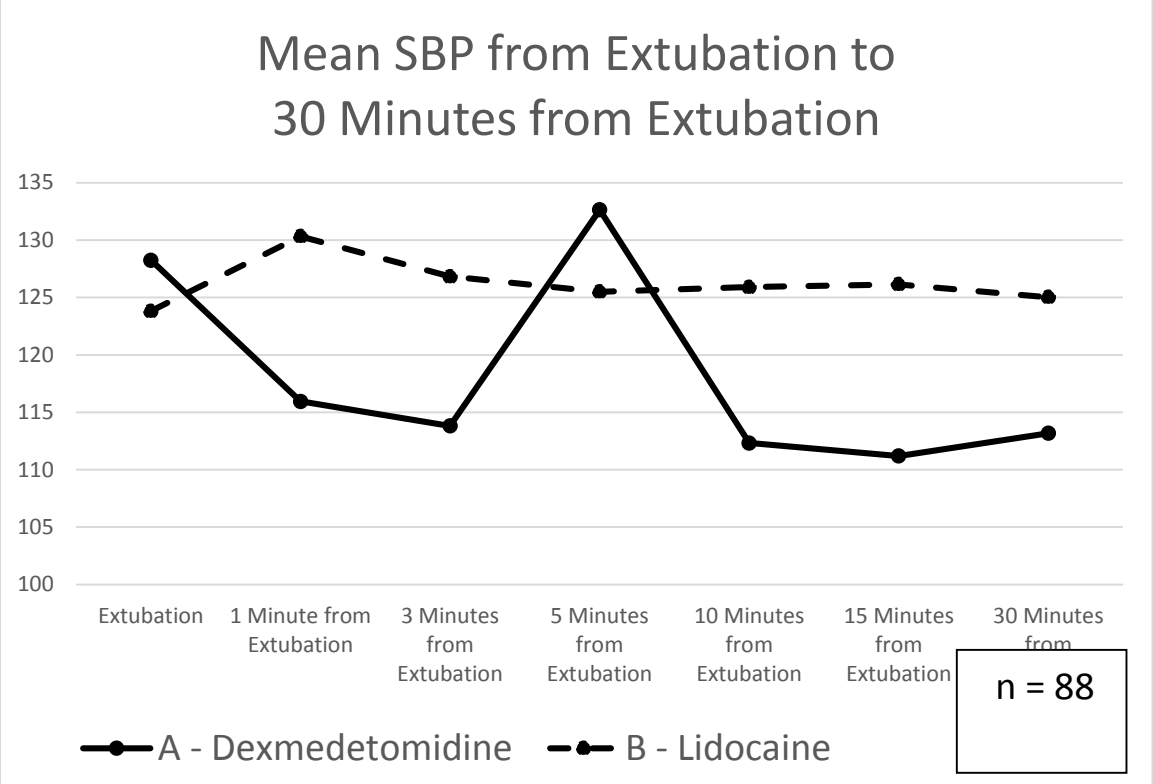
Average SBP	A Dexmedetomidine	B – Lidocaine	p value
Stoppage of Isoflurane	100.25	102.30	0.451
Reversal of Muscle Relaxant	104.86	115.52	0.004
Bolus Administration	113.32	117.02	0.298



Mean SBP from Extubation to 30 minutes from Extubation:

The mean SBP in mm Hg at extubation in Dexmedetomidine group was 128.25, and in Lidocaine group was 123.82. At 1 minute from extubation it was 115.95 in Dexmedetomidine group and 130.32 in Lidocaine group. At 3 minutes from extubation it was 113.82 in Dexmedetomidine group and 126.82 in Lidocaine group. At 5 minutes from extubation it was 132.64 in Dexmedetomidine group and 125.50 in Lidocaine group. At 10 minutes from extubation it was 112.32 in Dexmedetomidine group and 125.91 in Lidocaine group. At 15 minutes from extubation it was 111.20 in Dexmedetomidine group and 126.14 in Lidocaine group. At 30 minute from extubation it was 113.18 in Dexmedetomidine group and 125.02 in Lidocaine group.

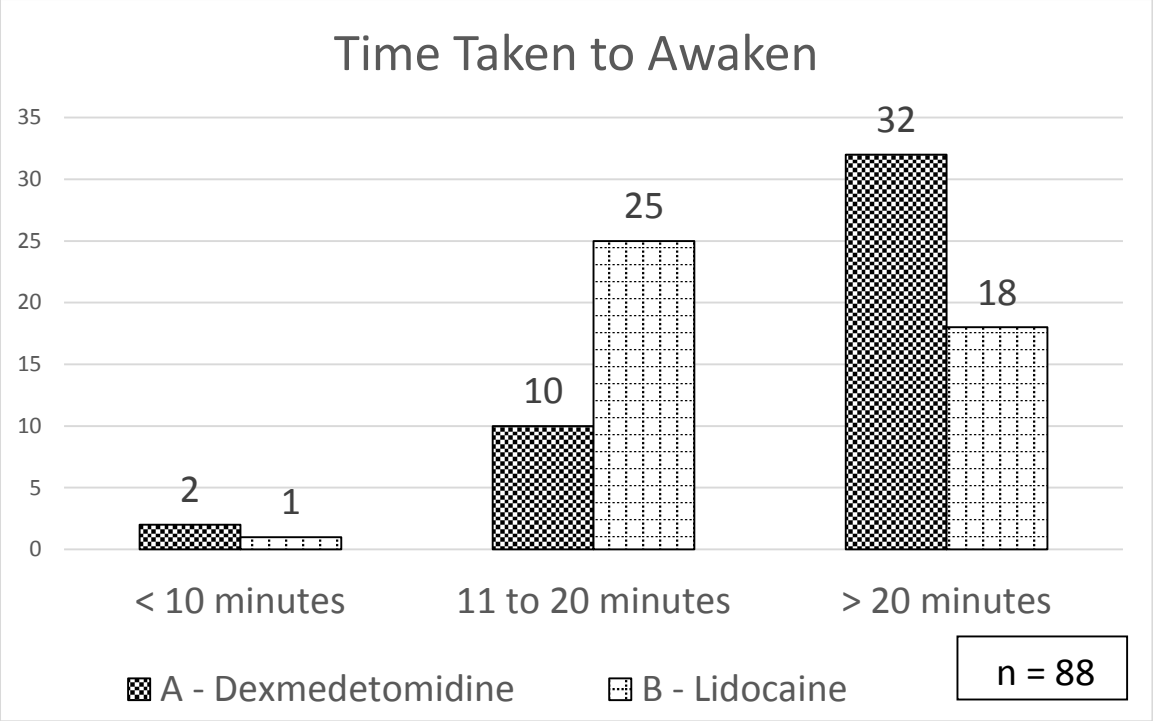
Mean SBP	A - Dexmedetomidine	B – Lidocaine	p value
Extubation	128.25	123.82	0.811
1 Minute from Extubation	115.95	130.32	0.000
3 Minute from Extubation	113.82	126.82	0.000
5 Minute from Extubation	132.64	125.50	0.700
10 Minute from Extubation	112.32	125.91	0.000
15 Minute from Extubation	111.20	126.14	0.000
30 Minute from Extubation	113.18	125.02	0.000



Time Taken to Awaken:

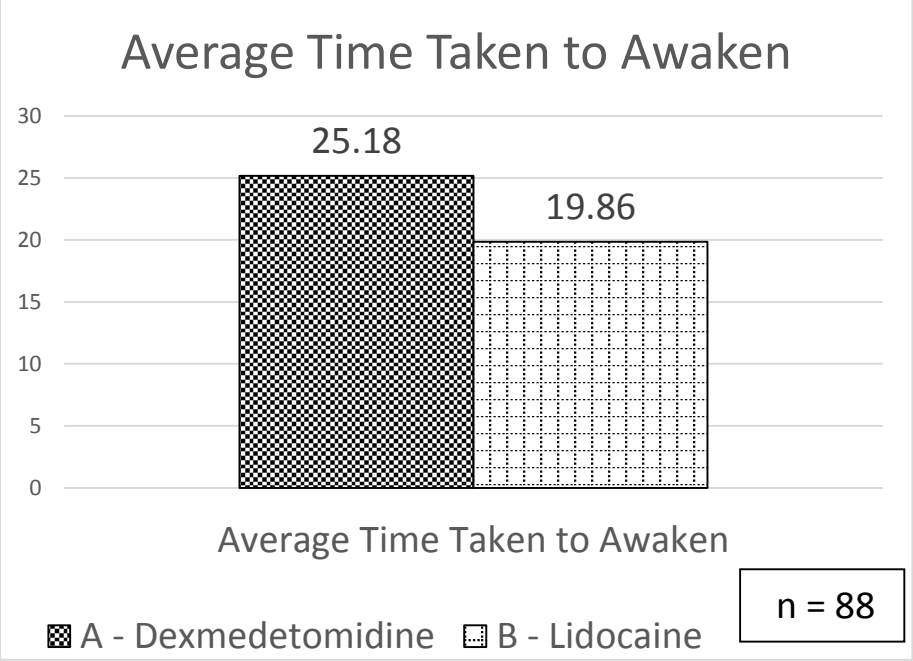
In Dexmedetomidine group, 2 patients took less than 10 minutes to awaken, 10 patients took between 11 and 20 minutes to awaken, and 32 patients took more than 20 minutes to awaken. In Lidocaine group, 1 patient took less than 10 minutes to awaken, 25 patients took between 11 and 20 minutes to awaken, and 18 patients took more than 20 minutes to awaken.

Time Taken to Awaken	A - Dexmedetomidine	B - Lidocaine	p value
<10 minutes	2	1	0.557
11 – 20 minutes	10	25	0.001
>20 minutes	32	18	0.003



The average time taken to awaken in Dexmedetomidine group was 25.18 minutes, and in Lidoacine group, it was 19.86 minutes.

	A - Dexmedetomidine	B - Lidocaine	p value
Average Time Taken to Awaken	25.18	19.86	0.000



DISCUSSION:

There was equal number of allocation in both the groups. The intended number for a power 80 was 43 in each arm, and there were 44 in each arm analysed. By randomisation, patients in both the groups were fairly matched with respect to age, gender, ASA status, comorbidities and body mass index. The indication for surgery, type of operation and the duration of operation did not vary much between the groups.

There was no significant association between cough at extubation and allergy, smoking, tracheal compression, duration of surgery and usage of stylet for intubation.

Propofol was used towards extubation in 7 patients (4 patients moved, 3 patients had grade 2 cough), and all patients belonged to Lidocaine arm. Patients may have responded to stimulus due to skin suturing, or the endotracheal tube as isoflurane was stopped when closure started, and the MAC started decreasing. There was no such occurrence in Dexmedetomidne arm. This is a significant difference with respect to blunting response during emergence from general anaesthesia (p value = 0.025). This could probably be due to the observation that Dexmedetomidine attenuates hemodynamic responses to tracheal intubation, decreases plasma catecholamine concentrations during anaesthesia, decreases peri-operative requirements for inhaled anaesthetics and opioids. (58) (1)

The incidence of cough during emergence from general anaesthesia in the presence of endotracheal tube has been observed as ranging between 38 and 96%. (17) (18). In our study, the overall incidence of cough at extubation is 51% (45/88 in both

groups combined). But the incidence of significant cough at extubation is only 12.5% (11/88).

Qing Fan et al (43) studied Dexmedetomidine and Remifentanil in preventing cough during extubation in patients undergoing ear surgeries. Smooth extubation without cough was achieved in 88% (22/25 patients) with 0.7 mcg/kg Dexmedetomidine. In our study, extubation without significant cough was achieved in 88.6% (39/44 patients) with 1 mcg/kg of Dexmedetomidine, which is similar to the observation by Qing Fan et al.

Yukioka H et al (64) found the incidence of coughing to be 0% (0/20 patients) with 2.0 mg/kg Lidocaine in patients undergoing obstetric, urologic, gynaecologic and general surgeries. In our study, significant coughing with 2 mg/kg Lidocaine was observed in 13.6% (6/44 patients). The probable reason for the higher incidence of cough is the type of surgery, because in thyroid surgeries the dissection around the trachea can itself cause irritation and increase the likelihood of occurrence of cough.

Ashraf MA Moustafa et al (53) compared the efficacy of the Dexmedetomidine and Lidocaine during extubation. Smooth extubation without cough or with minimal cough was achieved in 75% (15/20 patients) with 1 mg/kg Lidocaine, and 30% (6/20 patients) with 0.1 mcg/kg Dexmedetomidine, (p value <0.05), stating that there is significant difference between the two.

Sharma VB, Prabhakar H et al (65) compared Dexmedetomidine and Lidocaine in preventing airway responses during extubation in patients undergoing elective spine surgeries. They reported that there was no cough at extubation in 80% (16/20 patients) with Dexmedetomidine 0.5 mcg/kg, and in 65% (13/20 patients) with Lidocaine 1.5

mg/kg. Hence Dexmedetomidne and Lidocaine were comparable in preventing cough during extubation (p value = 0.288).

In our study, extubation with no cough or mild cough was achieved in 88.6% (39/44 patients) with 1 mcg/kg Dexmedetomidine, and in 86.4% (38/44 patients) with 2 mg/kg Lidocaine, with no significant difference (p value 0.891). The difference of observation between these studies is due to difference in the dose of the drugs used.

Only 5/44 patients (11.4%) had grade 3 (moderate) cough in Dexmedetomidine group, and only 6/44 patients (13.6%) had grade 3 (moderate) cough in Lidocaine group. No patient had grade 4 (severe) cough in both groups. Hence, both Dexmedetomidine and Lidocaine are found to be effective and equal in preventing cough at extubation.

Post extubation, only 1/44 patients (2.3%) had grade 3 (moderate) cough in Dexmedetomidine group, whereas, 4/44 patients (9.1%) had grade 3 (moderate) cough in Lidocaine group. There is no significant difference between Dexmedetomidine and Lidocaine in preventing post extubation cough (p value = 0.167). No patient had grade 4 (severe) cough on both the groups post extubation.

Although the mechanism by which intravenous lidocaine suppresses respiratory and laryngeal reflex responses is largely unknown, possible effects may include general anaesthesia, depression of motor function and direct blockade of noxious stimuli (60). A reflex response to laryngeal stimulation is mediated at subcortical level and therefore, a cortical effect may not be adequate to reduce the response to laryngeal stimulation. (70). Respiratory and laryngeal reflex responses elicited 10 minutes after the intravenous administration of lidocaine were different from those elicited

2 minutes after administration, even though Bispectral index values were similar at these two time intervals. So a direct anaesthetic effect of lidocaine does not sufficiently explain the mechanism of suppression of response to laryngeal stimulation. (60) (70). Lidocaine may cause suppression of cough by causing depression of brain stem functions. Lidocaine may also act by anaesthetising cough receptors in the hypopharynx and trachea. (61). Administration of intravenous lidocaine may suppress chemically and mechanically induced airway reflexes, including cough reflex. (61).

Dexmedetomidine is well known to attenuate haemodynamic responses to tracheal intubation, and it is also used for sedation in post-operative critically ill patients with ETT in situ. It causes co-operative conscious sedation by stimulating the locus coeruleus in the brain stem, resulting in inhibition of the sympathetic vasomotor centre of the brain as compared to other sedatives which act upon GABA-ergic pathways causing decrease or loss of consciousness. (71). Dexmedetomidine decreases acetylcholine release during cholinergic electrical field stimulation in the airway and may provide a probable mechanism for the observed use of Dexmedetomidine in attenuating airway reactivity during manipulation. (71). Dexmedetomidine also decreases C-fibre mediated airway smooth muscle contraction, which may probably be an underlying mechanism for cough suppression by dexmedetomidine. (71).

Dexmedtomidine significantly produced a stable heart rate trend during emergence compared to Lidocaine. There was no significant difference in the heart rate between the two groups at the time of reversal of muscle relaxant, at the time of

extubation, and at 30 minutes from extubation. At the time of administration of reversal, the tachycardia caused by the glycopyrrolate could have narrowed the difference between the two groups.

Ashraf MA Moustafa et al (53) compared haemodynamic responses between Dexmedetomidine and Lidocaine in hypertensive patients undergoing orthopaedic surgeries. They observed that HR and MAP increased temporarily after tracheal extubation in patients receiving Lidocaine. However, these hemodynamic changes were suppressed in those receiving Dexmedetomidine.

We have observed that, compared to Lidocaine, Dexmedetomidine significantly produced a stable heart rate, mean arterial pressure and systolic blood pressure during emergence, which was similar to the observation by Ashraf MA Moustafa et al. (53)

Sharma VB, Prabhakar H et al (65) studied Dexmedetomidine and Lidocaine in preventing airway and haemodynamic responses during extubation in patients undergoing elective spine surgeries. They observed that the time taken for emergence was 7.7 ± 3.8 minutes in Dexmedetomidine group, and in Lidocaine group it was 6.5 ± 1.9 minutes, hence no difference between the two (p value = 0.1).

In our study there was significant difference in time taken to awaken between the two groups. On an average, patients in Dexmedetomidine arm took 5.32 minutes more to awaken than did patients in Lidocaine arm. The difference in such observation from the above mentioned study is probably due to the difference in the dose of Dexmedetomidine used.

LIMITATIONS:

In our study, we did not include a placebo arm to compare both Dexmedetomidine and Lidocaine with placebo. We used historical cohort to assume the standard rate of emergence cough. This may not be situation in our institution as every place has a refined way of extubation and hence the incidence may be different. Different doses of dexmetomidine was not used to study the dose dependent effects.

CONCLUSION:

Both Dexmedetomidine at 1 mcg/kg and Lidocaine at 2 mg/kg are effective and equal in preventing cough during extubation.

Dexmedetomidine significantly attenuates haemodynamic response during emergence compared to Lidocaine.

Dexmetomidine helped to prevent early movement and cough towards the end of the surgery, but lidocaine did not always guarantee this.

Dexmedetomidine caused significant delay in awakening compared to Lidocaine.

Dexmedetomidine is a useful adjuvant to help in smooth extubation for head and neck surgery where one would want to minimise post-operative bleeding, though there is a slight delay in awakening. Future studies comparing different doses of Dexmedetomidine and Lidocaine with a placebo arm may be needed to ascertain and compare the effect of these drugs in preventing cough during emergence from general anaesthesia in surgeries where bleeding in the postoperative period is detrimental.

REFERENCES:

1. Barash P. Clinical Anaesthesia by Barash - 7th Edition. 7th ed. Vol. 1. Lippincot;

2. Polverino M, Polverino F, Fasolino M, Andò F, Alfieri A, De Blasio F. Anatomy and neuro-pathophysiology of the cough reflex arc. Multidiscip Respir Med. 2012 Jun 18;7(1):5.

3. Irwin RS, Corrao WM, Pratter MR. Chronic persistent cough in the adult: the spectrum and frequency of causes and successful outcome of specific therapy. Am Rev Respir Dis. 1981 Apr;123(4 Pt 1):413–7.

4. Decalmer SC, Webster D, Kelsall AA, McGuinness K, Woodcock AA, Smith JA. Chronic cough: how do cough reflex sensitivity and subjective assessments correlate with objective cough counts during ambulatory monitoring? Thorax. 2007 Apr;62(4):329–34.

5. Morice A, Geppetti P. Cough · 5: The type 1 vanilloid receptor: a sensory receptor for cough. Thorax. 2004 Mar;59(3):257–8.

6. Groneberg DA, Niimi A, Dinh QT, Cosio B, Hew M, Fischer A, et al. Increased Expression of Transient Receptor Potential Vanilloid-1 in Airway Nerves of Chronic Cough. Am J Respir Crit Care Med. 2004 Dec 15;170(12):1276–80.

7. McCool FD. Global Physiology and Pathophysiology of Cough. CHEST. 2006 Jan 1;129(1):48S–53S.

8. Ford PA, Barnes PJ, Usmani OS. Chronic cough and Holmes-Adie syndrome. Lancet Lond Engl. 2007 Jan 27;369(9558):342.

9. Irwin RS, Glomb WB, Chang AB. Habit cough, tic cough, and psychogenic cough in adult and pediatric populations: ACCP evidence-based clinical practice guidelines. Chest. 2006 Jan;129(1 Suppl):174S–179S.

10. Miller KA, Harkin CP, Bailey PL. Postoperative tracheal extubation. Anesth Analg. 1995 Jan;80(1):149–72.

11. Patel RI, Hannallah RS, Norden J, Casey WF, Verghese ST. Emergence airway complications in children: a comparison of tracheal extubation in awake and deeply anesthetized patients. Anesth Analg. 1991 Sep;73(3):266–70.

12. Caplan RA, Posner KL, Ward RJ, Cheney FW. Adverse respiratory events in anesthesia: a closed claims analysis. Anesthesiology. 1990 May;72(5):828–33.

13. Kim ES, Bishop MJ. Cough during emergence from isoflurane anesthesia. Anesth Analg. 1998 Nov;87(5):1170–4.

14. Leech P, Barker J, Fitch W. Proceedings: Changes in intracranial pressure and systemic arterial pressure during the termination of anaesthesia. Br J Anaesth. 1974 Apr;46(4):315–6.

15. Diachun CA, Tunink BP, Brock-Utne JG. Suppression of cough during emergence from general anesthesia: laryngotracheal lidocaine through a modified endotracheal tube. J Clin Anesth. 2001 Sep;13(6):447–51.

16. Mendel P, Fredman B, White PF. Alfentanil suppresses coughing and agitation during emergence from isoflurane anesthesia. J Clin Anesth. 1995 Mar;7(2):114–8.

17. Fagan C, Frizelle HP, Laffey J, Hannon V, Carey M. The effects of intracuff lidocaine on endotracheal-tube-induced emergence phenomena after general anesthesia. Anesth Analg. 2000 Jul;91(1):201–5.

18. Gonzalez RM, Bjerke RJ, Drobycki T, Stapelfeldt WH, Green JM, Janowitz MJ, et al. Prevention of endotracheal tube-induced coughing during emergence from general anesthesia. Anesth Analg. 1994 Oct;79(4):792–5.

19. Patel R, Norden J, Hannallah RS. Oxygen administration prevents hypoxemia during post-anesthetic transport in children. Anesthesiology. 1988 Oct;69(4):616–8.

20. Irwin RS, Baumann MH, Bolser DC, Boulet L-P, Braman SS, Brightling CE, et al. Diagnosis and management of cough executive summary: ACCP evidence-based clinical practice guidelines. Chest. 2006 Jan;129(1 Suppl):1S–23S.

21. Bidwai AV, Bidwai VA, Rogers CR, Stanley TH. Blood-pressure and pulse-rate responses to endotracheal extubation with and without prior injection of lidocaine. Anesthesiology. 1979 Aug;51(2):171–3.

22. Canning BJ. Anatomy and neurophysiology of the cough reflex: ACCP evidence-based clinical practice guidelines. Chest. 2006 Jan;129(1 Suppl):33S–47S.

23. Sant'Ambrogio G, Remmers JE, de Groot WJ, Callas G, Mortola JP. Localization of rapidly adapting receptors in the trachea and main stem bronchus of the dog. Respir Physiol. 1978 Jun;33(3):359–66.

24. Widdicombe JG. Afferent receptors in the airways and cough. Respir Physiol. 1998 Oct;114(1):5–15.

25. Giddings AE. The history of thyroidectomy. J R Soc Med. 1998;91(Suppl 33):3–6.

26. Wychulis AR, Beahrs OH, Woolner LB. Metastasis of Carcinoma to the Thyroid Gland. Ann Surg. 1964 Aug;160(2):169–77.

27. Rosato L, Avenia N, Bernante P, De Palma M, Gulino G, Nasi PG, et al. Complications of thyroid surgery: analysis of a multicentric study on 14,934 patients operated on in Italy over 5 years. World J Surg. 2004 Mar;28(3):271–6.

28. Bononi M, Amore Bonapasta S, Vari A, Scarpini M, De Cesare A, Miccini M, et al. Incidence and circumstances of cervical hematoma complicating thyroidectomy and its relationship to postoperative vomiting. Head Neck. 2010 Sep;32(9):1173–7.

29. Burkey SH, van Heerden JA, Thompson GB, Grant CS, Schleck CD, Farley DR. Reexploration for symptomatic hematomas after cervical exploration. Surgery. 2001 Dec 1;130(6):914–20.

30. Zelcer J, Wells DG. Anaesthetic-related recovery room complications. Anaesth Intensive Care. 1987 May;15(2):168–74.

31. Burkey SH, van Heerden JA, Thompson GB, Grant CS, Schleck CD, Farley DR. Reexploration for symptomatic hematomas after cervical exploration. Surgery. 2001 Dec;130(6):914–20.

32. Lang BH-H, Yih PC-L, Lo C-Y. A Review of Risk Factors and Timing for Postoperative Hematoma After Thyroidectomy: Is Outpatient Thyroidectomy Really Safe? World J Surg. 2012 Oct;36(10):2497–502.

33. Reeve T, Thompson NW. Complications of thyroid surgery: how to avoid them, how to manage them, and observations on their possible effect on the whole patient. World J Surg. 2000 Aug;24(8):971–5.

34. Promberger R, Ott J, Kober F, Koppitsch C, Seemann R, Freissmuth M, et al. Risk factors for postoperative bleeding after thyroid surgery. Br J Surg. 2012 Mar;99(3):373–9.

35. Shaha AR, Jaffe BM. Practical management of post-thyroidectomy hematoma. J Surg Oncol. 1994 Dec;57(4):235–8.

36. Harding J, Sebag F, Sierra M, Palazzo FF, Henry J-F. Thyroid surgery: postoperative hematoma--prevention and treatment. Langenbecks Arch Surg Dtsch Ges Für Chir. 2006 Jun;391(3):169–73.

37. Calò PG, Pisano G, Piga G, Medas F, Tatti A, Donati M, et al. Postoperative hematomas after thyroid surgery. Incidence and risk factors in our experience. Ann Ital Chir. 2010 Oct;81(5):343–7.

38. Chen E, Cai Y, Li Q, Cheng P, Ni C, Jin L, et al. Risk factors target in patients with post-thyroidectomy bleeding. Int J Clin Exp Med. 2014 Jul 15;7(7):1837–44.

39. Valley RD, Freid EB, Bailey AG, Kopp VJ, Georges LS, Fletcher J, et al. Tracheal extubation of deeply anesthetized pediatric patients: a comparison of

desflurane and sevoflurane. Anesth Analg. 2003 May;96(5):1320–1324, table of contents.

40. Venkatesan T, Korula G. A comparative study between the effects of 4% endotracheal tube cuff lignocaine and 1.5 mg/kg intravenous lignocaine on coughing and hemodynamics during extubation in neurosurgical patients: a randomized controlled double-blind trial. J Neurosurg Anesthesiol. 2006 Oct;18(4):230–4.

41. Navarro LHC, Lima RM e, Aguiar AS, Braz JRC, Carness JM, Módolo NSP. The effect of intracuff alkalinized 2% lidocaine on emergence coughing, sore throat, and hoarseness in smokers. Rev Assoc Medica Bras 1992. 2012 Apr;58(2):248–53.

42. Jee D, Park SY. Lidocaine sprayed down the endotracheal tube attenuates the airway-circulatory reflexes by local anesthesia during emergence and extubation. Anesth Analg. 2003 Jan;96(1):293–297, table of contents.

43. Fan Q, Hu C, Ye M, Shen X. Dexmedetomidine for tracheal extubation in deeply anesthetized adult patients after otologic surgery: a comparison with remifentanil. BMC Anesthesiol [Internet]. 2015 Jul 23 [cited 2017 Sep 20];15. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4511974/

44. Hartley M, Vaughan RS. Problems associated with tracheal extubation. Br J Anaesth. 1993 Oct;71(4):561–8.

45. Stone JG, Foëx P, Sear JW, Johnson LL, Khambatta HJ, Triner L. Risk of myocardial ischaemia during anaesthesia in treated and untreated hypertensive patients. Br J Anaesth. 1988 Dec;61(6):675–9.

46. Shajar MA, Thompson JP, Hall AP, Leslie NA, Fox AJ. Effect of a remifentanil bolus dose on the cardiovascular response to emergence from anaesthesia and tracheal extubation. Br J Anaesth. 1999 Oct;83(4):654–6.

47. Fujii Y, Kihara S, Takahashi S, Tanaka H, Toyooka H. Calcium channel blockers attenuate cardiovascular responses to tracheal extubation in hypertensive patients. Can J Anaesth J Can Anesth. 1998 Jul;45(7):655–9.

48. Dyson A, Isaac PA, Pennant JH, Giesecke AH, Lipton JM. Esmolol attenuates cardiovascular responses to extubation. Anesth Analg. 1990 Dec;71(6):675–8.

49. Fuhrman TM, Ewell CL, Pippin WD, Weaver JM. Comparison of the efficacy of esmolol and alfentanil to attenuate the hemodynamic responses to emergence and extubation. J Clin Anesth. 1992 Dec;4(6):444–7.

50. Nishina K, Mikawa K, Maekawa N, Obara H. Fentanyl attenuates cardiovascular responses to tracheal extubation. Acta Anaesthesiol Scand. 1995 Jan;39(1):85–9.

51. Nishina K, Mikawa K, Shiga M, Maekawa N, Obara H. Prostaglandin E1 attenuates the hypertensive response to tracheal extubation. Can J Anaesth J Can Anesth. 1996 Jul;43(7):678–83.

52. Nishina K, Mikawa K, Maekawa N, Obara H. Attenuation of cardiovascular responses to tracheal extubation with diltiazem. Anesth Analg. 1995 Jun;80(6):1217–22.

53. Moustafa AM, Atalla H, Koptan HM. Comparison of dexmedetomidine, lidocaine, and their combination in attenuation of cardiovascular and catecholamine responses to tracheal extubation and anesthesia emergence in hypertensive patients. Res Opin Anesth Intensive Care. 2015 Apr 1;2(2):1.

54. Frost EAM. Differential diagnosis of delayed awakening from general anesthesia: a review. Middle East J Anaesthesiol. 2014 Oct;22(6):537–48.

55. Misal US, Joshi SA, Shaikh MM. Delayed recovery from anesthesia: A postgraduate educational review. Anesth Essays Res. 2016;10(2):164–72.

56. Parr SM, Robinson BJ, Glover PW, Galletly DC. Level of consciousness on arrival in the recovery room and the development of early respiratory morbidity. Anaesth Intensive Care. 1991 Aug;19(3):369–72.

57. Steward DJ, Volgyesi G. Stabilometry: a new tool for the measurement of recovery following general anaesthesia for out-patients. Can Anaesth Soc J. 1978 Jan;25(1):4–6.

58. Miller R. Miller's Anesthesia - 7th Edition. 7th ed. Vol. 1.

59. Stoelting R. Pharmacology and Physiology in Anesthetic Practice. 4th Edition.

60. Erb TO, von Ungern-Sternberg BS, Keller K, Frei FJ. The effect of intravenous lidocaine on laryngeal and respiratory reflex responses in anaesthetised children*. Anaesthesia. 2013 Jan 1;68(1):13–20.

61. Gecaj-Gashi A, Nikolova-Todorova Z, Ismaili-Jaha V, Gashi M. Intravenous lidocaine suppresses fentanyl-induced cough in Children. Cough Lond Engl. 2013 Aug 15;9:20.

62. Steinhaus JE, Gaskin L. A study of intravenous lidocaine as a suppressant of cough reflex. Anesthesiology. 1963 Jun;24:285–90.

63. R. Smith F, C Kundahl P. Intravenously Administered Lidocaine as Cough Depressant during General Anesthesia for Bronchography. Chest. 1973 Apr 1;63:427–9.

64. Yukioka H, Yoshimoto N, Nishimura K, Fujimori M. Intravenous lidocaine as a suppressant of coughing during tracheal intubation. Anesth Analg. 1985 Dec;64(12):1189–92.

65. Prabhakar H, Rath G, Bithal P, Sharma V. Comparison of dexmedetomidine and lignocaine on attenuation of airway and pressor responses during tracheal extubation. J Neuroanaesth Crit Care. 2014;1(1):50.

66. Aksu R, Akin A, Biçer C, Esmaoğlu A, Tosun Z, Boyaci A. Comparison of the effects of dexmedetomidine versus fentanyl on airway reflexes and hemodynamic responses to tracheal extubation during rhinoplasty: A double-blind, randomized, controlled study. Curr Ther Res Clin Exp. 2009 Jun;70(3):209–20.

67. Abou-Madi MN, Keszler H, Yacoub JM. Cardiovascular reactions to laryngoscopy and tracheal intubation following small and large intravenous doses of lidocaine. Can Anaesth Soc J. 1977 Jan;24(1):12–9.

68. Poulton TJ, James FM. Cough suppression by lidocaine. Anesthesiology. 1979 May;50(5):470–2.

69. Thorén P, Oberg B. Studies on the endoanesthetic effects of lidocaine and benzonatate on non-medullated nerve endings in the left ventricle. Acta Physiol Scand. 1981 Jan;111(1):51–8.

70. Kim W-Y, Lee Y-S, Ok S-J, Chang M-S, Kim J-H, Park Y-C, et al. Lidocaine does not prevent bispectral index increases in response to endotracheal intubation. Anesth Analg. 2006 Jan;102(1):156–9.

71. Mikami M, Zhang Y, Kim B, Worgall TS, Groeben H, Emala CW. Dexmedetomidine's inhibitory effects on acetylcholine release from cholinergic nerves in guinea pig trachea: a mechanism that accounts for its clinical benefit during airway irritation. BMC Anesthesiol [Internet]. 2017 Mar 29 [cited 2017 Oct 12];17. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5372301/

ANNEXURES:

OFFICE OF RESEARCH
INSTITUTIONAL REVIEW BOARD (IRB)
CHRISTIAN MEDICAL COLLEGE, VELLORE, INDIA

Ethics Committee Registration No: ECR/326/INST/TN/2013 issued under Rule 122D of the Drugs & Cosmetics Rules 1945, Govt. of India

March 09, 2017,

Dr. Charles J,
PG Registrar,
Department of Anesthesia,
Christian Medical College,
Vellore 632 004.

Sub: **Fluid Research Grant: New Proposal:**
Comparison of Dexmedetomidine and Lidocaine in Preventing Cough During Emergence from General Anaesthesia for Thyroidectomy.
Dr. Charles J, Employment Number: 29234, PG Resident, Department of Anaesthesiology, Dr. Tony Thomson Chandy, Employment Number: 20236 Professor, Dr. Suma Mary Thampi – Associate Professor, Employment Number: 28608, Dr. Deepak Thomas Abraham – Professor & Head, Employment Number: 20130, Dr. M J Paul – Professor, Dr. Anish Jacob Cherian – Assistant Professor, Employment Number: 28558, Anaesthesiology.

Ref: IRB Min No: 10551 [INTERVEN] dated 15.02.2017

Dear Dr. Charles J,

I enclose the following documents:-

1. Institutional Review Board approval 2. Agreement

Could you please sign the agreement and send it to Dr. Biju George, Addl. Vice Principal (Research), so that the grant money can be released.

With best wishes,

Dr. Biju George
Secretary (Ethics Committee)
Institutional Review Board

Dr. BIJU GEORGE
MBBS., MD., DM.
SECRETARY - (ETHICS COMMITTEE)
Institutional Review Board,
Christian Medical College, Vellore - 632 002.

Cc: Dr. Tony Thomson Chandy, Department of Anaesthesia, CMC, Vellore. 1 of 5

Ethics Committee Silver, Office of Research, I Floor, Carman Block, Christian Medical College, Vellore, Tamil Nadu 632 002
Tel: 0416 – 2284294, 2284202 Fax: 0416 – 2262788 E-mail: research@cmcvellore.ac.in

OFFICE OF RESEARCH
INSTITUTIONAL REVIEW BOARD (IRB)
CHRISTIAN MEDICAL COLLEGE, VELLORE, INDIA

Ethics Committee Registration No: ECR/326/INST/TN/2013 issued under Rule 122D of the Drugs & Cosmetics Rules 1945, Govt. of India

Dr. George Thomas, M.B.B.S., D. Ortho., Ph.D.,
Chairperson, Ethics Committee

Dr. B. Antonisamy, M.Sc., Ph.D., FSMS, FRSS.,
Secretary, Research Committee

Prof. Keith Gomez, B.Sc., MA (S.W), M.Phil.,
Deputy Chairperson, Ethics Committee

Dr. Anna Benjamin Pulimood, M.B.B.S., MD., Ph.D.,
Chairperson, Research Committee & Principal

Dr. Biju George, M.B.B.S., MD., DM.,
Deputy Chairperson,
Secretary, Ethics Committee, IRB
Additional Vice-Principal (Research)

March 09, 2017,

Dr. Charles J,
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Ref: IRB Min No: 10551 [INTERVEN] dated 15.02.2017

Dear Dr. Charles J,

The Institutional Review Board (**Silver**, Research and Ethics Committee) of the Christian Medical College, Vellore, reviewed and discussed your project titled "Comparison of Dexmedetomidine and Lidocaine in Preventing Cough During Emergence from General Anaesthesia for Thyroidectomy" on February 15th 2017.

The Committee reviewed the following documents

1. IRB Application format
2. Consent forms and Information sheets
3. Proforma
4. Cvs of Drs. Anish, Charles, Deepak, MJ Paul, Rekha, Suma, Tony.
5. GCP Certificate
6. No. of documents 1 – 5.

The following Institutional Review Board (**Silver**, Research & Ethics Committee) members were present at the meeting held on February 15th 2017 in the BRTC Conference Room, Christian Medical College, Bagayam, Vellore 632002.

2 of 5

Name	Qualification	Designation	Affiliation
Dr. B. Antonisamy	MSc, PhD, FSMS, FRSS	Professor, Biostatistics, Secretary (ResearchCommittee), IRB, CMC, Vellore	Internal, Statistician
Dr. George Thomas	MBBS, D Ortho, PhD	Orthopaedic Surgeon, St. Isabella Hospital, Chennai, Chairperson, Ethics Committee, IRB, Chennai	External, Clinician
Dr. Jayaprakash Muliyil	BSc, MBBS, MD, MPH, Dr PH (Epid), DMHC	Retired Professor, Vellore	External, Scientist &Epidemiologist
Dr. Anuradha Bose	MBBS, DCH, MD, MRCP, FRCPCH	Professor, Community Medicine, CMC, Vellore	Internal, Clinician
Dr. Biju George	MBBS, MD, DM	Professor, Haematology, Additional Vice Principal (Research), Deputy Chairperson (Research Committee), Member Secretary (Ethics Committee), IRB, CMC, Vellore.	Internal, Clinician
Dr. Suceena Alexander	MBBS, MD, DM	Associate Professor, Nephrology, CMC, Vellore	Internal, Clinician
Prof. Keith Gomez	BSc, MA (S.W), M. Phil (Psychiatry Social Work)	Student counselor, Loyola College, Chennai, Deputy Chairperson, Ethics Committee, IRB	External, Lay Person & Social Scientist
Dr. P. Zachariah	MBBS, PhD	Retired Professor, Vellore	External, Clinician
Dr. D. J. Christopher	BSc, MBBS, DTCD DNB, FRCP(Glasg), FCCP(USA)	Professor, Pulmonary Medicine, CMC, Vellore	Internal, Clinician
Mr. C. Sampath	BSc, BL	Advocate, Vellore	External, Legal Expert

Ethics Committee Silver, Office of Research, I Floor, Carman Block, Christian Medical College, Vellore, Tamil Nadu 632 002
Tel: 0416 – 2284294, 2284202 Fax: 0416 – 2262788 E-mail: research@cmcvellore.ac.in

Dr. Shirley David	MSc, PhD	Professor,Head of Fundamentals Nursing Department, College of Nursing, CMC, Vellore	Internal, Nurse
Mrs. Ruma Nayak	M Sc (Nursing)	Professor, Head of Paediatric Nursing & Deputy Nursing Superintendent, College of Nursing, CMC, Vellore	Internal, Nurse
Dr. Prasanna Samuel	MSc, PhD	Lecturer, Biostatistics, CMC, Vellore	Internal, Statistician
Dr. Suresh Devasahayam	BE, MS, PhD	Professor of Bio-Engineering, CMC, Vellore	Internal, Basic Medical Scientist
Mrs. Pattabiraman	BSc, DSSA	Social Worker, Vellore	External, Lay Person
Dr. Abhay Gahukamble	MS, D Ortho, DNB(Ortho)	Associate Professor, Paediatric Orthopaedics, CMC, Vellore	Internal, Clinician
Dr. Ashish Goel	MBBS, MD, DM	Professor, Hepatology, CMC, Vellore	Internal, Clinician
Dr. Jiji Elizabeth Mathews	MBBS, DGO, MD,	Professor, Obstetrics & Gynaecology, CMC, Vellore	Internal, Clinician

We approve the project to be conducted as presented.

Kindly provide the total number of patients enrolled in your study and the total number of withdrawals for the study entitled: "Comparison of Dexmedetomidine and Lidocaine in Preventing Cough During Emergence from General Anaesthesia for Thyroidectomy" on a monthly basis. Please send copies of this to the Research Office (research@cmcvellore.ac.in).

The Institutional Ethics Committee expects to be informed about the progress of the project, any **adverse events** occurring in the course of the project, any **amendments in the protocol and the patient information / informed consent**. On completion of the study you are expected to submit a copy of the **final report**. Respective forms can be downloaded from the following link: http://172.16.11.136/Research/IRB_Polices.html in the CMC Intranet and in the CMC website link address: http://www.cmch-vellore.edu/static/research/Index.html.

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Fluid Grant Allocation:

A sum of 50,000/- INR(Rupees Fifty Thousand only) will be granted for 6 months.

Yours sincerely

Dr. Biju George
Secretary (Ethics Committee)
Institutional Review Board

Dr. BIJU GEORGE
MBBS., M[illegible] DM.
SECRETARY - (ETHICS COMMITTEE)
Institutional Review Board,
Christian Medical College, Vellore - 632 002.

Ethics Committee Silver, Office of Research, I Floor, Carman Block, Christian Medical College, Vellore, Tamil Nadu 632 002
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Consent to Take Part in a Clinical Trial

Study Title:
Comparison of Dexmedetomidine and Lidocaine in Preventing Cough During Emergence from General Anaesthesia for Thyroidectomy

Study Number:

Participant's Name:

Date of Birth / Age (in years):

I, _____

_____, Son / Daughter of _____

(Please tick boxes)

Declare that I have read the information sheet provided to me regarding this study and have clarified any doubts that I had. [ ]

I also understand that my participation in this study is entirely voluntary and that I am free to withdraw permission to continue to participate at any time without affecting my usual treatment or my legal rights [ ]

I also understand that neither I, nor my doctors, will know which drug I will receive (Lidocaine or Dexmedetomidine) [ ]

I understand that I will receive free treatment for any study related injury or adverse event but I will not receive and other financial compensation [ ]

I understand that the study staff and institutional ethics committee members will not need my permission to look at my health records even if I withdraw from the trial. I agree to this access [ ]

I understand that my identity will not be revealed in any information released to third parties or published [ ]

I agree to pay for any investigation routinely warranted for my treatment [ ]

I voluntarily agree to take part in this study [ ]

Name: Signature:

Date:

Name of witness: Signature:

Relation to participant: Date:

Name of the Doctor: Signature:

Date:

Christian Medical College, Vellore

Department of Anaesthesia

Comparison of Dexmedetomidine and Lidocaine in Preventing Cough During Emergence from General Anaesthesia for Thyroidectomy: Double Blinded Randomized Controlled Study

Information sheet

You are invited to be part of a study to improve the current knowledge regarding the role of drugs to prevent cough while waking up general anaesthesia for thyroid removal operation. This study will help other patients who later come to hospital for the same operation. By agreeing to be a part of this study, you will contribute to scientific knowledge.

The information collected from you will include

1. History – This includes details regarding your general health and the disease for which you are undergoing the operation.
2. Clinical Examination – Besides the regular doctors rounds, the primary investigator and the treating anaesthesiologist will examine you.

You will be examined post operatively by the treating anaesthesiologist in the ward and data will be collected and analysed.

Whether you accept or decline to be a part of this study will not affect your further treatment in this hospital.

Although you may not directly benefit by enrolling in this study, you will be contributing to scientific knowledge.

You are scheduled to undergo total / hemi thyroidectomy under general anaesthesia. Considering the type of surgery and anaesthesia, you have a risk of suffering from cough at the end of surgery, which further can cause bleeding from operation site. The current recommendation of therapy does not involve administration of any drug to prevent cough. The idea of this research is to study and compare the effects of two drugs, namely Lidocaine and Dexmedetomidine (both given as injection), to prevent cough. By being a part of the study you will be randomly allotted into two groups. In one group, patients will receive Dexmedetomidine and the second group patients will receive Lidocaine. Both of these regimens are well studied and are routinely used during operations to prevent stress response. The operative technique and all other anaesthetic approaches will be similar. The occurrence of cough will be observed and treated accordingly as usual.

We wish to study this in detail and are therefore conducting a scientific study.

All details including personal data, assessment of the doctor during and after the operation will be kept confidential.

These drugs will be given free of cost to you. The rest of the treatment cost will be the same as discussed with your surgery unit doctors.

Participation in this study is purely voluntary, and you can withdraw from the study at any time, and that refusal to participate will not involve any penalty or loss of benefits to which you are otherwise entitled.

PROTOCOL SHEET

- No sedative premedication on the day prior to surgery or on the day of surgery
- Standard monitors for intraoperative monitoring as per ASA guidelines
- Induction of anaesthesia with Fentanyl 2 mcg/kg, Propofol 2 mg/kg, Atracurium 0.5 mg/kg
- No Lidocaine at intubation
- Size 6.5 ETT for female and size 7.0 ETT for male
- ETT cuff pressure measured after intubation and the same kept between 20 to 30 cm of water
- Dexamethasone 0.1 mg/kg IV after intubation
- Isoflurane for maintenance of anaesthesia – MAC maintained between 0.8 to 1.0
- Analgesia with Paracetamol 15 mg/kg (up to 1 g), Fentanyl up to 5 mcg/kg
- No Morphine / Tramadol / Diclofenac / Regional Analgesia
- Intermittent Atracurium for muscle relaxation as required
- Study drug infusion started when closure of muscle layer started
- The infusion rate set as body weight in ml/hour and stopped in 15 minutes
- Isoflurane stopped when closure of skin started
- Fresh gas flow increased and Reversal of muscle relaxant administered when the skin closure ended
- Study drug bolus given as body weight/10 ml when MAC reached 0.3
- ETT cuff pressure measured at MAC 0.3, and kept between 20 to 30 cm of water
- No calling or touching or stimulating the patient in any way
- Patients waited upon to breathe, open eyes / make purposeful movement

- Shoulder roll / head ring not removed until shifting the patient to trolley
- Oral suction given only after the patient awakened and then ETT removed
- Occurrence of cough at extubation, 1 minute from extubation, 3 minutes from extubation, 5 minutes from extubation, 10 minutes from extubation, 15 minutes from extubation, 30 minutes from extubation and in PACU recorded
- Haemodynamic responses (heart rate and blood pressure) also recorded at the same time points
- Time taken to awaken calculated from the time of stoppage of isoflurane to the time of extubation
- Data recorded in proforma with all timings
- Grade 3 or grade 4 cough - treated with Propofol and the same recorded in the proforma

Clinical Trial Details (PDF Generation Date :- Thu, 23 Mar 2017 16:03:30 GMT)

CTRI Number	CTRI/2017/03/008193 [Registered on: 23/03/2017] - **Trial Registered Prospectively**
Last Modified On	16/03/2017
Post Graduate Thesis	Yes
Type of Trial	Interventional
Type of Study	Drug Surgical/Anesthesia
Study Design	Randomized, Parallel Group, Multiple Arm Trial
Public Title of Study	Comparison between two medicines namely Dexmedetomidine and Lidocaine to Prevent Cough while waking up from General Anaesthesia in Thyroid Gland Surgery
Scientific Title of Study	Comparison of Dexmedetomidine and Lidocaine in Preventing Cough During Emergence from General Anaesthesia for Thyroidectomy

Secondary IDs if Any

Secondary ID	Identifier
NIL	NIL

Details of Principal Investigator or overall Trial Coordinator (multi-center study)

Details of Principal Investigator	
Name	Charles J
Designation	PG Resident
Affiliation	Christian Medical College, Vellore.
Address	Department of Anaesthesiology, Christian Medical College, Vellore. Vellore TAMIL NADU 632004 India
Phone	9894095907
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Email	chaarless2000@rediffmail.com

Details Contact Person (Scientific Query)

Details Contact Person (Scientific Query)	
Name	Tony Thomson Chandy
Designation	Professor
Affiliation	Christian Medical College, Vellore.
Address	Department of Anaesthesiology, Christian Medical College, Vellore. Vellore TAMIL NADU 632004 India
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Details Contact Person (Public Query)

Details Contact Person (Public Query)	
Name	Charles J
Designation	PG Resident
Affiliation	Christian Medical College, Vellore.
Address	Department of Anaesthesiology, Christian Medical College, Vellore. Vellore TAMIL NADU 632004 India
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Email	chaarless2000@rediffmail.com

Source of Monetary or Material Support

Source of Monetary or Material Support
> Institutional Fluid Research Grant, Office of Research, Christian Medical College, Vellore, Tamil Nadu. PIN - 632002.

Primary Sponsor

Primary Sponsor Details	
Name	Christian Medical College Vellore
Address	Christian Medical College, Vellore, Tamil Nadu, India. PIN - 632004.
Type of Sponsor	Research institution and hospital

Details of Secondary Sponsor

Name	Address
NIL	NIL

Countries of Recruitment

List of Countries
India

Sites of Study

Name of Principal Investigator	Name of Site	Site Address	Phone/Fax/Email
Charles J	Christian Medical College Hospital Vellore	Endocrine Surgery Operating Rooms, Main Operation Theatre Complex, Christian Medical College Hospital Vellore Tamil Nadu India PIN 632004 Vellore TAMIL NADU	9894095907 chaarless2000@rediffmail.com

Details of Ethics Committee

Name of Committee	Approval Status	Date of Approval	Is Independent Ethics Committee?
Ethics Committee Silver, CMC Vellore	Approved	09/03/2017	No

Regulatory Clearance Status from DCGI

Status	Date
Not Applicable	No Date Specified

Health Condition / Problems Studied

Health Type	Condition
Patients	Cough

Intervention / Comparator Agent

Type	Name	Details
Intervention	Dexmedetomidine	Administered intravenously as 1 mcg/kg infusion over 15 minutes. It is just once administered dose only.
Comparator Agent	Lidocaine	Administered intravenously as 2 mg/kg bolus. It is just once administered dose only.

Inclusion Criteria

Inclusion Criteria	
Age From	18.00 Year(s)
Age To	70.00 Year(s)
Gender	Both
Details	All adult patients for thyroidectomy ASA I, II, III Patients given consent for the trial

Exclusion Criteria

Exclusion Criteria	
Details	Patients not given consent Baseline Heart Rate Uncontrolled Systemic Hypertension Patients with Tracheomalacia

	Patients on Antiarrhthmic Drugs
Method of Generating Random Sequence	Permuted block randomization, variable
Method of Concealment	Sequentially numbered, sealed, opaque envelopes
Blinding/Masking	Participant, Investigator and Outcome Assessor Blinded

Primary Outcome

Outcome	Timepoints
Cough During Emergence from General Anaesthesia	At Extubation and at 1, 3, 5, 10, 15, 30 minutes from Extubation

Secondary Outcome

Outcome	Timepoints
Heart Rate Blood Pressure	At Extubation and at 1, 3, 5, 10, 15, 30 minutes from Extubation

Target Sample Size	**Total Sample Size=**100 **Sample Size from India=**100
Phase of Trial	N/A
Date of First Enrollment (India)	24/03/2017
Date of First Enrollment (Global)	No Date Specified
Estimated Duration of Trial	**Years=**0 **Months=**6 **Days=**0
Recruitment Status of Trial (Global)	Not Applicable
Recruitment Status of Trial (India)	Not Yet Recruiting
Publication Details	NA

Brief Summary

Structured Abstract:

Background: Postoperative neck haematoma requiring emergent surgical evacuation is a rare but dreaded complication of thyroidectomy as the mortality rate is high. Bleeding frequently occurs in the case of sudden violent cough, sneeze or vomit, especially during extubation. So, it is reasonable to take measures to prevent cough during emergence from general anaesthesia, so as to prevent the possible life threatening complication of post thyroidectomy neck haematoma causing airway compromise and possibly death. Dexmedetomidine has been successfully used to attenuate the haemodynamic responses to tracheal intubation and extubation, in doses ranging between 0.5 mcg/kg to 1 mcg/kg. Lidocaine has also been used in doses between 1 mg/kg to 2 mg/kg to prevent cough during emergence from general anaesthesia. Studies are not available till date comparing these drugs in preventing cough in thyroidectomy.

Aim: Primary: To compare the effect of Dexmedetomidine and Lidocaine

in preventing cough during emergence from general anaesthesia for thyroidectomy

Secondary: a) To compare the effect of Dexmedetomidine and Lidocaine in attenuating haemodynamic responses during emergence from general anaesthesia for thyroidectomy

b) To compare the effect of Dexmedetomidine and Lidocaine on time taken to awaken from general anaesthesia for thyroidectomy

Design: Double Blinded Randomised Control Trial

Methods: Consent will be taken by the primary investigator after explaining the procedure in detail in the ward in the evening prior to the operation. Patients will be randomized in to two arms, the Dexmedetomidine arm and the Lidocaine arm. The patients will undergo the surgery as per routine. All anaesthetic agents and techniques will be standardised to eliminate confounding factors. Opaque, sealed envelope will be opened outside the operating room, and the drugs will be loaded appropriately and labeled with study number by an anaesthesiologist not involved in the study or the operation. Thus the treating anaesthesiologist is blinded. Dexmedetomidine will be diluted to 50 ml and 2% Lidocaine will be taken in 10 ml syringe. Group A will receive 1 mcg/kg of Dexmedetomidine (body weight in ml/hour for 15 minutes) and body weight/10 ml of normal saline. Group B will receive 2 mg/kg of Lidocaine (body weight/10 ml) and body weight in ml/hour of normal saline for 15 minutes. The infusion will be started when the closure of muscle layer starts and the bolus will be given when the MAC reaches 0.3. Heart Rate and Blood Pressure will be recorded prior to induction, every 5 minutes intra-operatively and every 2 minutes when the MAC reaches 0.3. Any occurrence of cough during emergence, extubation, in PACU will be recorded. Cough will be graded as, grade 1 – no cough, grade 2 – mild cough (one or two), grade 3 – moderate cough (three or four), grade 4 – heavy cough (five or more), grade 5 – severe cough (laryngospasm, no breathing). Propofol will be used as a rescue measure for severe cough, up to 1 mg/kg. Recordings will be made at extubation, and then at 1, 3, 5, 10, 15 and 30 minutes from extubation. Data collected will be entered in Epidata software and analysed.